PURINA Institute

Advancing Science for Pet Health

TECHNOLOGICALLY EMPOWERED VETERINARY CARE

PURINA INSTITUTE GLOBAL SUMMIT 2025

At The Forefront Of Companion Animal Science

30 April - 1 May 2025

Table of Contents

Applying Big Data, Machine Learning, and AI to Improve Nutrition and Health

Audrey Ruple, DVM, MS, PhD, DACVPM, Virginia-Maryland College of Veterinary Medicine, VA, USA
aruple@vt.edu

Julia Labadie, DVM, MSPH, PhD, Morris Animal Foundation, CO, USA,
jlabadie@morrisanimalfoundation.org

Daniel Promislow, DPhil., Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

Glossary of Abbreviations

AI	artificial intelligence
DAP	Dog Aging Project
EMR	electronic medical record
GRLS	Golden Retriever Lifetime Study
ML	machine learning
TRIAD	Test of Rapamycin in Aging Dogs
WGS	whole genome sequencing

Introduction

Technologically empowered veterinary care is transforming the field of animal health. The integration of Big Data, Artificial Intelligence (AI), and Machine Learning (ML) enables practitioners and researchers to move beyond individual-level insights to population-level understanding, offering unprecedented opportunities to improve the health of companion animals. This overview will highlight current applications of Big Data and AI/ML in veterinary medicine and demonstrate how these tools are shaping the future of animal care.

The authors of this manuscript have been helping to lead two large-scale longitudinal studies–the Golden Retriever Lifetime Study[1,2] and the Dog Aging Project[3] – both of which have a central focus on the causes, processes and diseases of aging. Age is the greatest risk factor for most causes of mortality in both dogs and humans.[4,5] The causes and consequences of aging and age-related disease are exceedingly complex. As such, they lend themselves to a Big Data approach, which can capture the extraordinary diversity of factors associated with aging and age-related disease.

The past several decades of research on the biology of aging, or "geroscience", focused on laboratory-based studies of yeast, nematode worms, fruit flies, and other species, have uncovered genetic pathways that influence aging and cellular and molecular hallmarks of aging, all of which are deeply evolutionarily conserved.[6-9] However, these discoveries have been made in the highly controlled conditions of inbred animals living under laboratory conditions. We do not know to what extent these same factors might explain variation in aging among individuals within a natural population. It is here that Big Data, and statistical tools like AI and ML, can shed light on the causes and consequences of aging in the real world.

It makes good sense to focus our attention on aging in companion animals. They share many of the same aging-related diseases as humans, they share our environment, they are as genetically variable as human populations, and they benefit from a sophisticated health care system that provides disease diagnosis, prognosis, treatment and prevention. But their relatively short lives mean that we can make fundamental discoveries about aging in a relatively short amount of time. These commonalities and differences have motivated our own research, and have the potential to lead to fundamental discoveries about the causes of aging-related diseases and avenues for treatment and prevention in companion dogs, with the added benefit of having high translational potential to inform our understanding of aging in humans as well.

Harnessing Big Data in Veterinary Medicine

Big Data refers to extremely large datasets that are complex, diverse, and rapidly generated from a variety of sources, including electronic medical records (EMRs), wearable devices, environmental descriptors, genomics and other molecular 'omic' profiles, imaging, and owner-reported data. In veterinary medicine, the aggregation and analysis of such datasets can illuminate patterns that are not discernible through traditional methods.

Veterinary big data originate from several key sources, each offering unique insights into animal health. Medical record databases—such as those from Banfield Pet Hospital, the Veterinary Medical Database, the Small Animal Veterinary Surveillance Network (SAVSNET), and VetCompass—contain clinical and demographic information, and in some cases, include geocoded data that link animals to specific geographic locations.[10-13] These resources are invaluable for monitoring disease trends, studying antimicrobial resistance, and conducting large-scale epidemiological research.

Another important source of veterinary big data is insurance databases. These datasets are typically large in scale and provide detailed information not only about the animals but also about their owners and environments. Such data have been widely used in studies investigating morbidity and mortality, with prominent examples including the Agria database in Sweden and Pet Protect in the UK.[14,15] The combination of medical and insurance data supports a more holistic understanding of animal health and its many influencing factors.

Large-scale cohort studies such as the Dog Aging Project (DAP) and the Golden Retriever Lifetime Study (GRLS) (see details below) exemplify how Big Data is being used to study canine health over time.[2,3] These datasets provide longitudinal, multi-modal information, offering a window into aging, disease progression, and lifestyle factors that influence health outcomes. Both studies collect detailed longitudinal information across domains such as diet, behavior, molecular profiles, and medical history, enabling insights into how lifestyle factors influence health outcomes over the life course, and the mechanisms by which they do so, for a large and diverse group of dogs.[16] In addition, the DAP has integrated multi-level environmental and behavioral data using geocoded survey responses to examine how external factors like the built environment and access to greenspace impact health trajectories in dogs.[17] These datasets enable AI models to be applied across complex domains, such as examining correlations between nutrition, environmental factors, molecular traits, and disease occurrence.

Artificial Intelligence and Machine Learning Applications

The application of AI and ML in veterinary medicine, especially in health prediction, has rapidly expanded due to the availability of large datasets. These techniques allow researchers to analyze complex, high-dimensional data and uncover patterns that are not easily visible through traditional statistical methods.

Machine learning algorithms have been effectively used to predict health outcomes in dogs using large-scale insurance claims data. For example, Debes et al.[18] used insurance claims data from over 785,000 dogs to accurately predict health outcomes in 45 different disease categories, incorporating features like breed, age, sex, and environmental exposures in the predictive models. These models are not only valuable for identifying dogs at increased risk of disease but can also support proactive care and tailored nutritional recommendations aimed at improving health outcomes.[18]

Similarly, pet insurance data have been used in a One Health context to model disease trends in both dogs and humans. O'Brien et al.[19] demonstrated how canine insurance data could be used to predict vector-borne and zoonotic diseases such as Lyme disease and giardiasis in people, showing that trends in dog disease incidence often precede human trends by one to two years.[19] These findings underscore the utility of AI tools in using canine data to support early intervention strategies that benefit both human and animal health.

Collectively, these real-world applications show that AI and ML approaches, when applied to robust and representative datasets, can significantly advance veterinary nutrition and health by supporting personalized care strategies and improving disease prevention efforts.

Over the past 15 years, there has been a surge of work using ML approaches to study aging, including analysis of medical imaging, the study of brain networks using fMRI, facial aging,[20] and the search for drugs that might extend healthspan or lifespan.[21] But the greatest attention has been paid to the development of so-called 'biological clocks' that many have argued can measure intrinsic, biological age. This work was stimulated in large part by two 2013 papers on epigenetic clocks.[22,23] These models use high-dimensional measures of methylation patterns across the genome, taken from large numbers of known-age individuals. Machine learning models are then used to estimate the age of each individual (***Figure 1***). Departure from the predicted age is assumed to be a measure of the biological age of an individual.

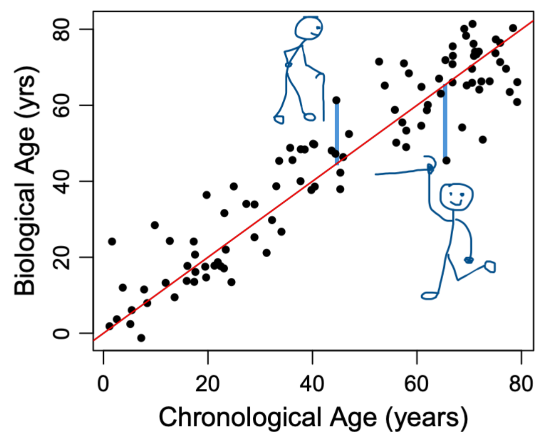


Figure 1. Model of biological clock. Each point represents an individual, with their predicted epigenetic age ('biological age') shown on the Y axis. Points above the isometric (red) line are thought to have accelerated age, while those below the line are intrinsically younger than their chronological age.

These studies launched a veritable cottage industry, testing these clocks in diverse populations around the world, and building next-generation biological clocks in the hope of increasing their predictive power. This is a new field, and has attracted attention not only by many proponents, but also by those raising concerns about the design and interpretations of these biomarkers of aging.[24-26] Despite these challenges, they have illustrated the power of ML approaches to identify biomarkers of aging. In the past several years, with a tremendous increase in the amount of available data from human populations, researchers have begun to explore computationally intensive AI approaches to discover ever more accurate predictors of disease and death.[27,28]

Of note, many of those working on the search for biomarkers are interested in *surrogate* biomarkers of aging.[29,30] Ideally, with a small biospecimen, one could measure the intrinsic state of aging in an organism, and thus also be able to quickly determine if an intervention, be it dietary, pharmacological, or otherwise, might delay or decrease the effect of aging on morbidity and mortality. Given the challenge of testing interventions to slow aging in relatively long-lived organisms, it is not surprising that there is so much interest in the discovery of surrogate biomarkers.

The combination of Big Data and extraordinary computational power is creating new and exciting opportunities to study aging. Until now, most of the effort in this field has been targeted at data either from human populations or lab-based model organisms. As we make clear in the next section, there are now exceptional opportunities to bring these tools to bear on veterinary cohorts.

Open Data Resources in Geroscience and Veterinary Medicine

The Open Data movement has created a strong impetus to create large datasets publicly, and often freely, available, and the geroscience community has benefited greatly from this movement. Among the many powerful resources are data from long-term longitudinal studies like the Framingham Heart Study[31] and the Baltimore Longitudinal Study,[32] the Health and Retirement Study,[33] and the UK Biobank,[34] as well as repositories that store multiple aging-related datasets, such as the Elite Portal (). Here we describe two specific veterinary resources, the Golden Retriever Lifetime Study and the Dog Aging Project, which are just beginning to reveal the potential of AI/ML analyses of Big Data to generate tremendous insights into biological variation in companion dogs.

The Golden Retriever Lifetime Study is one of the largest, most comprehensive longitudinal veterinary cohort studies, following 3,044 Golden Retrievers in the contiguous United States.[2] The primary aim of the study is to investigate risk factors for cancer and other common diseases in dogs, with an emphasis on lymphoma, osteosarcoma, hemangiosarcoma, and high-grade mast cell tumors. Rolling enrollment of dogs aged 6 months through 2 years was conducted from 2012–2015. Extensive owner- and veterinarian-completed annual questionnaires obtain information about lifestyle, environmental exposures, physical activity, reproductive history, behavior, diet, medications, and diagnoses. Dogs also have annual veterinary examinations and biospecimen collection (whole blood, serum, hair, nails, feces, urine) for laboratory analysis and biobanking. The cohort was genotyped using a 1.1 million marker Axiom array and a subset of dogs also have whole genome sequencing data. As of April 2025, 507 hemangiosarcomas, 209 lymphoma/leukemias, 45 high-grade mast cell tumors, and 37 osteosarcomas have been diagnosed. When possible, we also obtain tumor samples for biobanking. Additionally, many other disorders common in Golden Retrievers have been diagnosed, including otitis externa, atopy, hypothyroidism, cataracts, and orthopedic disorders. A subset of questionnaire data and all our genotyping data are freely available to researchers through our Data Commons site (https://datacommons.morrisanimalfoundation.org). In addition, researchers can apply to access additional data and/or biospecimens through our request for proposal process (https://www.morrisanimalfoundation.org/bette-m-morris-data-commons-biorepository).

The Dog Aging Project (DAP) is a long-term longitudinal study designed to examine the genetic and environmental factors that influence aging and age-related traits, and the mechanisms by which they do so. The project launched in 2019, and has since recruited more than 50,000 dogs of all ages, sizes, and breeds (including both purebred and mixed breed dogs), from all across the United States. For dogs in the primary cohort, known as the DAP Pack, owners fill out surveys that describe the health, behavior, diet, and environment of their dog. A summary of data from the Pack is provided in a data dashboard (https://data.dogagingproject.org/). For each dog, in addition to owner-reported in-home environmental data, addresses are used to identify extra-local environmental measures, such as air quality, nearest parks, neighborhood deprivation indices, annual weather patterns, and much more.[17,35,36] Nested within the Pack are several sampled cohorts, including the Foundation Cohort (6000 dogs with whole genome sequencing [WGS)), the Precision Cohort (976 dogs, with WGS, as well as annual measures of the microbiome, epigenome, metabolome, immunophenotype, and CBC/Chem/UA profiling),[37] and an Intervention Cohort, known as TRIAD (for Test of Rapamycin In Aging Dogs). Dogs in TRIAD are part of a double-masked placebo-controlled clinical trial testing the ability of rapamycin to increase healthy longevity.[38] For the majority of dogs, including all those in sampled cohorts, veterinary electronic medical records are available. A Dog Aging Project biobank includes tens of thousands of biospecimens that are also available to the research community.[39] Researchers can apply for access to the DAP data through the project's website (https://dogagingproject.org/data-access).

Conclusion

The convergence of Big Data, AI, and ML represents a paradigm shift in veterinary medicine. These technologies empower the profession to move from reactive to proactive care, unlocking insights that can inform more effective nutritional and health interventions. As we continue to explore the applications of these tools, interdisciplinary collaboration and responsible innovation will be essential to realizing their full potential.

Conflicts of Interest

Audrey Ruple is the Chair of the Veterinary Advisory Board of Fetch Pet Insurance, a compensated position. Daniel Promislow serves as a consultant for WndrHLTH Club, Inc.

References

1. Guy, M. K., Page, R. L., Jensen, W. A., Olson, P. N., Haworth, J. D., Searfoss, E. E., & Brown, D. E. (2015). The Golden Retriever Lifetime Study: establishing an observational cohort study with translational relevance for human health. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *370*(1673), 20140230. doi: 10.1098/rstb.2014.0230
2. Labadie, J., Swafford, B., DePena, M., Tietje, K., Page, R., & Patterson-Kane, J. (2022). Cohort profile: The Golden Retriever Lifetime Study (GRLS). *PloS One*, *17*(6), e0269425. doi: 10.1371/journal.pone.0269425
3. Creevy, K. E., Akey, J. M., Kaeberlein, M., Promislow, D. E. L., & Dog Aging Project Consortium. (2022). An open science study of ageing in companion dogs. *Nature*, *602*(7895), 51–57. doi: 10.1038/s41586-021-04282-9
4. Creevy, K. E., Austad, S. N., Hoffman, J. M., O'Neill, D. G., & Promislow, D. E. L. (2016). The Companion Dog as a Model for the Longevity Dividend. *Cold Spring Harbor Perspectives in Medicine*, *6*(1), a026633.
5. Hoffman, J. M., Creevy, K. E., Franks, A., O'Neill, D. G., & Promislow, D. E. L. (2018). The companion dog as a model for human aging and mortality. *Aging Cell*, *17*(3), e12737. doi: 10.1111/acel.12737
6. Fontana, L., Partridge, L., & Longo, V. D. (2010). Extending Healthy Life Span—From Yeast to Humans. *Science*, *328*(5976), 321–326. doi: 10.1126/science.1172539
7. Kennedy, B. K., Berger, S. L., Brunet, A., Campisi, J., Cuervo, A. M., Epel, E. S., Franceschi, C., Lithgow, G. J., Morimoto, R. I., Pessin, J. E., Rando, T. A., Richardson, A., Schadt, E. E., Wyss-Coray, T., & Sierra, F. (2014). Geroscience: linking aging to chronic disease. *Cell*, *159*(4), 709–713. doi: 10.1016/j.cell.2014.10.039
8. López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The hallmarks of aging. *Cell*, *153*(6), 1194–1217. doi: 10.1016/j.cell.2013.05.039
9. Tartiere, A. G., Freije, J. M. P., & López-Otín, C. (2024). The hallmarks of aging as a conceptual framework for health and longevity research. *Frontiers in Aging*, *5*, 1334261. doi: 10.3389/fragi.2024.1334261

10. Bartlett, P. C., Van Buren, J. W., Neterer, M., & Zhou, C. (2010). Disease surveillance and referral bias in the veterinary medical database. *Preventive Veterinary Medicine*, *94*(3-4), 264–271. doi: 10.1016/j.prevetmed.2010.01.007
11. *State of Pet Health®*. (n.d.). Banfield Pet Hospital®. Retrieved April 2, 2025, from https://www.banfield.com/State-of-pet-health
12. *Using SAVSNET data for research*. (n.d.). University of Liverpool. Retrieved April 2, 2025, from https://www.liverpool.ac.uk/savsnet/using-savsnet-data-for-research/
13. *VetCompass - Overview*. (n.d.). Retrieved May 1, 2021, from http://www.rvc.ac.uk/vetcompass/about
14. Dobson, J. M., Samuel, S., Milstein, H., Rogers, K., & Wood, J. L. N. (2002). Canine neoplasia in the UK: estimates of incidence rates from a population of insured dogs. *The Journal of Small Animal Practice*, *43*(6), 240–246. doi: 10.1111/j.1748-5827.2002.tb00066.x
15. Egenvall, A., Nødtvedt, A., Penell, J., Gunnarsson, L., & Bonnett, B. N. (2009). Insurance data for research in companion animals: benefits and limitations. *Acta Veterinaria Scandinavica*, *51*(1), 42. doi: 10.1186/1751-0147-51-42
16. Paynter, A. N., Dunbar, M. D., Creevy, K. E., & Ruple, A. (2021). Veterinary Big Data: When Data Goes to the Dogs. *Animals : An Open Access Journal from MDPI*, *11*(7), 1872. doi: 10.3390/ani11071872
17. Xue, D., Collins, C., Kauffman, M., Dunbar, M., Crowder, K., Schwartz, S., Ruple, A., & Dog Aging Project Consortium. (2022). Big data from small animals: Integrating multi-level environmental data in the Dog Aging Project. *OIE Scientific and Technical Review*, *41*(2). doi: 10.20506/rst.42.3349
18. Debes, C., Wowra, J., Manzoor, S., & Ruple, A. (2023). Predicting health outcomes in dogs using insurance claims data. *Scientific Reports*, *13*(1), 9122. doi: 10.1038/s41598-023-36023-5
19. O'Brien, J., McCullough, A., Debes, C., & Ruple, A. (2024). Using pet insurance claims to predict occurrence of vector-borne and zoonotic disease in humans. In *medRxiv* (p. 2024.08. 09.24311752). doi: 10.1101/2024.08.09.24311752
20. Chen, W., Qian, W., Wu, G., Chen, W., Xian, B., Chen, X., Cao, Y., Green, C. D., Zhao, F., Tang, K., & Han, J.-D. J. (2015). Three-dimensional human facial morphologies as robust aging markers. *Cell Research*, *25*(5), 574–587. doi: 10.1038/cr.2015.36
21. Arora, S., Mittal, A., Duari, S., Chauhan, S., Dixit, N. K., Mohanty, S. K., Sharma, A., …Ahuja, G. (2025). Discovering geroprotectors through the explainable artificial intelligence-based platform AgeXtend. *Nature Aging*, *5*(1), 144–161. doi: 10.1038/s43587-024-00763-4
22. Hannum, G., Guinney, J., Zhao, L., Zhang, L., Hughes, G., Sadda, S., Klotzle, B., Bibikova, M., Fan, J.-B., Gao, Y., Deconde, R., Chen, M., Rajapakse, I., Friend, S., Ideker, T., & Zhang, K. (2013). Genome-wide methylation profiles reveal quantitative views of human aging rates. *Molecular Cell*, *49*(2), 359–367. doi: 10.1016/j.molcel.2012.10.016
23. Horvath, S. (2013). DNA methylation age of human tissues and cell types. *Genome Biology*, *14*(10), R115. doi: 10.1186/gb-2013-14-10-r115. Erratum in *Genome Biology, 16*(1), 96. doi: 10.1186/s13059-015-0649-6
24. El Khoury, L. Y., Gorrie-Stone, T., Smart, M., Hughes, A., Bao, Y., Andrayas, A., Burrage, J., Hannon, E., Kumari, M., Mill, J., & Schalkwyk, L. C. (2019). Systematic underestimation of the epigenetic clock and age acceleration in older subjects. *Genome Biology*, *20*(1), 283. doi: 10.1186/s13059-019-1810-4
25. Koch, Z., Li, A., Evans, D. S., Cummings, S., & Ideker, T. (2025). Somatic mutation as an explanation for epigenetic aging. *Nature Aging*, online ahead of print. doi: 10.1038/s43587-024-00794-x
26. Watkins, S. H., Testa, C., Chen, J. T., De Vivo, I., Simpkin, A. J., Tilling, K., Diez Roux, A. V., Davey Smith, G., Waterman, P. D., Suderman, M., Relton, C., & Krieger, N. (2023). Epigenetic clocks and research implications of the lack of data on whom they have been developed: a review of reported and missing sociodemographic characteristics. *Environmental Epigenetics*, *9*(1), dvad005. doi: 10.1093/eep/dvad005
27. Biomarkers of Aging Consortium, Herzog, C. M. S., Goeminne, L. J. E., Poganik, J. R., Barzilai, N., Belsky, D. W., Betts-LaCroix, J., … Gladyshev, V. N. (2024). Challenges and recommendations for the translation of biomarkers of aging. *Nature Aging*, *4*(10), 1372–1383. doi: 10.1038/s43587-024-00683-3
28. Moqri, M., Herzog, C., Poganik, J. R., Ying, K., Justice, J. N., Belsky, D. W., Higgins-Chen, A. T., … Ferrucci, L. (2024). Validation of biomarkers of aging. *Nature Medicine*, *30*(2), 360–372. doi: 10.1038/s41591-023-02784-9
29. Cummings, S. R., & Kritchevsky, S. B. (2022). Endpoints for geroscience clinical trials: health outcomes, biomarkers, and biologic age. *GeroScience*, *44*(6), 2925–2931. doi: 10.1007/s11357-022-00671-8
30. LeBrasseur, N. K. (2024). Hungry for biomarkers of aging. *Aging Cell*, *23*(4), e14158. doi: 10.1111/acel.14158
31. D'Agostino Sr, R. B., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008).

General cardiovascular risk profile for use in primary care: The Framingham Heart Study. *Circulation, 117*(6), 743-753. doi: 10.1161/CIRCULATIONAHA.107.699579

32. Ferrucci, L. (2008). The Baltimore Longitudinal Study of Aging (BLSA): a 50-year-long journey and plans for the future. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *63*(12), 1416–1419. doi: 10.1093/gerona/63.12.1416
33. Sonnega, A., Faul, J. D., Ofstedal, M. B., Langa, K. M., Phillips, J. W. R., & Weir, D. R. (2014). Cohort profile: The health and Retirement Study (HRS). *International Journal of Epidemiology*, *43*(2), 576–585. doi: 10.1093/ije/dyu067
34. Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., Downey, P., ...Collins, R. (2015). UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Medicine*, *12*(3), e1001779. doi: 10.1371/journal.pmed.1001779
35. McCoy, B., Brassington, L., Dolby, G., Jin, K., Collins, D., Dunbar, M., & Snyder-Mackler, N. (2021). The link between environment, age, and health in a large cohort of companion dogs from the Dog Aging Project. *Innovation in Aging*, *5*(Supplement 1), 983–983. doi: 10.1093/geroni/igab046.3530
36. McCoy, B. M., Brassington, L., Jin, K., Dolby, G. A., Shrager, S., Collins, D., Dunbar, M., Dog Aging Project Consortium, Ruple, A., & Snyder-Mackler, N. (2023). Social determinants of health and disease in companion dogs: a cohort study from the Dog Aging Project. *Evolution, Medicine, and Public Health*, *11*(1), 187–201. doi: 10.1093/emph/eoad011.
37. Prescott, J., Keyser, A. J., Litwin, P., Dunbar, M. D., McClelland, R., Ruple, A., Ernst, H., … Promislow. (2025). Rationale and design of the Dog Aging Project precision cohort: a multi-omic resource for longitudinal research in geroscience. *GeroScience*, online ahead of print. doi: 10.1007/s11357-025-01571-3
38. Coleman, A. E., Creevy, K. E., Anderson, R., Reed, M. J., Fajt, V. R., Aicher, K. M., Atiee, G., … Dog Aging Project Consortium. (2025). Test of Rapamycin in Aging Dogs (TRIAD): study design and rationale for a prospective, parallel-group, double-masked, randomized, placebo-controlled, multicenter trial of rapamycin in healthy middle-aged dogs from the Dog Aging Project. *GeroScience*, online ahead of print. doi: 10.1007/s11357-024-01484-7
39. Mouttham, L., & Castelhano, M. G. (2022). Purpose, partnership, and possibilities: The implementation of the Dog Aging Project biobank. *Biomarker Insights*, *17*, 11772719221137217. doi: 10.1177/11772719221137217

Utilizing Smart Devices to Improve Comprehensive Weight Loss Programs for Pets

Jenessa A. Winston, DVM, PhD, DACVIM (Small Animal Internal Medicine)
The Ohio State University College of Veterinary Medicine, Ohio, United States of America
winston.210@osu.edu

Glossary of Abbreviations

LOAD Liverpool Osteoarthritis in Dogs questionnaire
QoL Quality of Life

Introduction

The obesity epidemic is rampant in companion animals, affecting 59% of dogs and 61% of cats in the United States alone.[1] Obesity results from a prolonged positive energy balance leading to expansion of adipose tissue and fat deposition in other organs, which promotes an "obesogenic" environment characterized by dysregulation of metabolic, hormonal, and inflammatory responses.[2,3] Ultimately these changes lead to physical impairment, comorbidities, and reduced quality of life and healthspan.[2,4]

Although obesity is a preventable disease, this growing epidemic is the most common nutritional disorder in companion animals and is associated with significant consequences.[5] Dogs and cats suffering from obesity experience a higher frequency of multiple devastating comorbidities including endocrine dysfunction (e.g. diabetes mellitus, hypothyroidism, hyperadrenocorticism, hyperlipidemia), cardiovascular disease (e.g. hypertension, collapsing trachea), orthopedic disease (e.g. osteoarthritis), renal and urinary disease, and neoplasia.[6] Furthermore, in a lifelong study in Labrador retrievers, even moderately overweight dogs were at greater risk for earlier morbidity and a shortened lifespan.[7] Reduced lifespan has also been documented in obese cats.[8]

To date, several epidemiologic studies have identified associations and risk factors for canine and feline obesity, which include animal factors (e.g. breed, neuter status, age) and owner factors (e.g. diet choice, feeding methods and practices, exercise and living environment, age and body composition of owner).[9,10] Veterinarians estimate that only 3% of obese pets are attributed to animal-specific factors, compared to 97% of obese pets being related to owner-specific factors.[11]

Traditionally, standard of care obesity management incorporates two major principles: calorie restriction (aka "*feed less*") and activity modification (aka "*exercise more*"). Despite veterinarian recommendations regarding dietary intervention and exercise, obesity remains a major companion animal health concern with an alarming acceleration in prevalence.[1,5] Recent research has focused on identifying obstacles to successful weight loss programs in pets, and owner compliance plays a huge role.[10,12] Identifying interventional solutions to overcome owner incompliance and enhance owner engagement and commitment to their pet's weight loss are critical to addressing obesity in companion animals. In human obesity clinical trials, technology-assisted (e.g. smart devices) weight loss interventions resulted in enhanced engagement compared to traditional weight loss programs.[13,14] Therefore, in companion animals, smart devices (such as wearable activity collars, digital automatic feeders, and litterbox monitors that serve as a digital scale) are examples of technology that when added to traditional weight loss programs may serve as an interventional solution to overcome these obstacles. This lecture will provide examples of smart devices utilized in successful weight loss programs in pets.

Smart Devices Used in Successful Weight Loss Programs in Dogs

To date, there are limited studies evaluating the use of smart devices in structured weight loss programs in dogs. Wearable activity monitors are increasingly used to evaluate canine activity. These devices are worn on the collar and collect data on daily activity patterns as well as estimate calories expended per day based on the pet's activity. Activity is tracked in different proprietary forms, usually with a daily goal being calculated based on owner-provided dog demographics. The device used in our studies[a] has been validated to track physical activity when dogs are off-leash, with one study demonstrating high correlational of dog step count to recorded activity.[15] However, the use of this smart device in dogs to track energy expenditure is unreliable.[16]

Recently, our research group sought to determine the utility of activity devices to monitor activity changes in obese dogs undergoing a structured weight loss program.[17] To do this, we leveraged data from the AKC Canine Health Foundation funded Canine SLIM study[18], a 24-week clinical trial aimed to study the effects of fecal microbiota transplants on obese dogs undergoing a structured weight loss program. The Canine SLIM study captured a comprehensive dataset including participants wearing an activity monitor throughout the 24-week study. While weight loss is widely believed to be associated with improved mobility, there are limited studies using activity monitors to examine mobility changes during structured weight loss programs in dogs. For this subproject of the Canine SLIM study, we aimed to analyze the relationship between the Liverpool Osteoarthritis in Dogs (LOAD) questionnaire scores (which assess owner-perceived mobility), quality of life (QoL) scores, and activity levels reported by the device. Over the 24 weeks, as dogs lost weight, we hypothesized that obese dogs would show an increase in reported activity levels, as well as an improvement in their QoL and LOAD scores. Owners completed a LOAD survey every 3 weeks and QoL survey every 12 weeks. Daily activity was tracked with the activity monitors. QoL scores and fold changes of monitor-recorded activity and LOAD scores were examined for changes over time. As dogs lost weight, results demonstrated improved physical dimension of QoL scores when comparing baseline to week 24 ($P=0.0075$). Significant changes in LOAD scores were noted between week 12 to 24 ($P<0.02$). No significant differences in weekly activity were observed over the 24-week study. These results demonstrate that weight loss improves owner perceived physical QoL parameters while maintaining mobility in obese dogs undergoing a weight loss program. The activity monitoring device provided a user-friendly platform to monitor activity levels in obese dogs undergoing a successful weight loss program.[17]

Based on this evidence, activity monitors should be considered when designing a technology-enhanced weight loss program for dogs. The role the smart device and its user platform provide for increasing owner compliance and engagement in a canine weight loss program needs to be investigated further.

Smart Devices Used in Successful Weight Loss Programs in Cats

To date, there are several studies that have evaluated various smart devices for use in weight loss programs in cats. Multiple-cat households are challenging for implementation of weight loss programs. Multiple-cat households pose a unique problem for calorie restriction in traditional weight loss programs, as food stealing, need for different foods, and variable feeding styles among housemates may influence compliance. The implementation of technology-enhanced weight loss programs in cats may be one way to overcome these obstacles.

For example, in one prospective study, 23 overweight/obese cats underwent a 6-month weight loss program which compared using a traditional feeding bowl with two meals fed per day to using an automatic feeder with two meals or six meals fed per day.[19] This calorie restricted program aimed for cats to lose between 0.5-1.5% of their body weight each week. In this study, overweight/obese cats that were fed from an automatic feeder were more likely to reach an ideal body condition (P=0.006), with 83.2% of cats fed six meals per day from automatic feeders and 40% of cats fed two meals per day from automatic feeders achieving ideal body condition. Importantly, no cats achieved an ideal body condition that were fed twice daily with a traditional bowl. Owners that utilized the automatic feeders reported that the weight loss plan was easier compared to owners using traditional bowls (P=0.01). Another obstacle to successful weight loss in cats is food-seeking behaviors, and in this study owners using automatic feeders, regardless of daily meal number (two versus six), reported fewer food-seeking incidences than cats fed with a traditional bowl. Overall, this study highlights that use of automatic feeders, which provide separation and portioned meals, lead to successful weight loss in cats.[19]

To add to these findings, another prospective study in 15 cats who underwent a 12-week weight loss program aimed to compare traditional dietary restriction alone to a technology-enhanced program including dietary restriction, digital scales, smart feeders, activity monitors, and pet treat cameras.[20] Owners with cats in the technology-enhanced group reported favorable feedback that smart feeders and home scales were a valuable addition to the program while activity monitors and pet treat cameras were less valuable. In this cohort, the average weekly weight loss was high in the technology group compared to the traditional dietary restriction group (P=0.036). This study provides evidence that technology-enhanced weight loss programs in cats can be accepted by cat owners and result in successful weight loss.[20]

Importantly, another component of a successful feline weight loss program are at-home accurate digital scales to avoid frequent veterinary visits for weekly weigh-ins. Litterbox scales are available to cat owners and are activated automatically when a cat uses the litterbox. A passive smart device (positioned under the cat's normal litterbox) can record body weight but can also predict urinary and defecation events. Recently, our research group sought to determine if a litterbox monitoring device[b] could be used in obese cats undergoing a structured weight loss program to accurately and passively record body weight.[17] To do this, we are leveraging the feline cohort from the Morris Animal Foundation funded Feline SLIM study, a 24-week clinical trial aimed to study the effects of fecal microbiota transplants on obese cats undergoing a structured weight loss program. The ongoing Feline SLIM study is capturing a comprehensive dataset, including some participants utilizing the litterbox monitoring device to record body weight at home. During this lecture, preliminary results from using the monitoring devices to passively evaluate feline body weight at home compared to a traditional digital scale will be shared. Incorporation of litterbox monitoring devices into technology-enhanced weight loss programs could help to reduce weekly weigh-ins critical to successful weight loss in cats. The role the device and user-platform provide for increasing owner compliance and engagement in a feline weight loss program needs to be investigated further.

Conclusion

Obesity is a growing epidemic in companion animals, which promotes an "obesogenic" environment characterized by dysregulation of metabolic, hormonal, and inflammatory responses. Ultimately these changes lead to physical impairment, comorbidities, and reduced quality of life and healthspan. Traditional approaches to obesity management (calorie restriction and exercise) can be augmented by adding in smart devices (such as wearable activity collars, digital automatic feeders, and litterbox monitors) to increase owner engagement and sustain owner commitment to weight loss programs for their pets. These technology-enhanced weight loss programs are one interventional solution to try to abate the obesity epidemic in companion animals.

Conflicts of Interest

Dr. Jenessa Winston is funded by a National Institute of Allergy and Infectious Disease Mentored Clinical Scientist Research Career Development Award under award number K08AI153550. Dr. Winston's laboratory has been funded by the EveryCat Health Foundation, the Morris Animal Foundation, the American Kennel Club's Canine Health Foundation, Nestle Purina, the FDA, and the National Institutes of Health. She has received speaker honoraria from Royal Canin, Nestle Purina, Blue Veterinary, and DVM360.

Footnotes:

[a] FitBark: FitBark, Inc. (Kansas City, MO, USA)

[b] Petivity Smart Litter Monitor: Nestlé Purina PetCare (St. Louis, MO, USA)

References

1. Ward, E. (2023). Survey reveals pet owners don't recognize excess weight, struggle with pet weight loss, and give lots of dog treats. Association for Pet Obesity Prevention. Available at https://www.petobesityprevention.org/articlesandnews/survey-reveals-pet-owners-dont-recognize-excess-weight-struggle-with-pet-weight-loss-and-give-lots-of-dog-treats.
2. Clark, M., & Hoenig, M. (2016). Metabolic effects of obesity and its interaction with endocrine diseases. *Veterinary Clinics of North America: Small Animal Practice, 46*(5), 797-815. doi: 10.1016/j.cvsm.2016.04.004
3. Torres-Fuentes, C., Schellekens, H., Dinan, T. G., & Cryan, J. F. (2017). The microbiota-gut-brain axis in obesity. *Lancet Gastroenterology Hepatology, 2*(10), 747-756. doi: 10.1016/S2468-1253(17)30147-4
4. Salt, C., Morris, P. J., Wilson, D., Lund, E. M. & German, A. J. (2019). Association between life span and body condition in neutered client-owned dogs. *Journal of Veterinary Internal Medicine, 33*, 89–99. doi: 10.1111/jvim.15367
5. Bartges, J., Kushner, R. F., Michel, K. E., Sallis, R. & Day, M. J. (2017). One Health solutions to obesity in people and their pets. *Journal of Comparative Pathology, 156*(4), 326–333. doi: 10.1016/j.jcpa.2017.03.008
6. Parker, V. (2019). Pathophysiology of obesity: Comorbidities and anesthetic considerations. In M. Cline & M. Murphy (Eds.), *Obesity in the Dog and Cat* (First edition). CRC Press. https://doi.org/10.1201/9781315151625
7. Kealy, R. D., Lawler, D. F., Ballam, J. M., Mantz, S. L., Biery, D. N., Greeley, E. H., Lust, G., …Stowe, H. D. (2002). Effects of diet restriction on life span and age-related changes in dogs. *Journal of the American Veterinary Medical Association, 220*(9), 1315-1320. doi:10.2460/javma.2002.220.1315
8. Teng, K. T., McGreevy, P. D., Toribio, J. L., Rabenheimer, D., Kendall, K., & Dhand, N K. (2018). Strong associations of nine-point body condition scoring with survival and lifespan in cats. *Journal of Feline Medicine and Surgery, 20*(12), 1110–1118. doi: 10.1177/1098612X17752198
9. Larsen, J. A., & Villaverde, C. (2016). Scope of the problem and perception by owners and veterinarians. *Veterinary Clinics of North America: Small Animal Practice, 46*(5), 761–772. doi: 10.1016/j.cvsm.2016.04.001
10. Cline, M. G., Burns, K. M., Coe, J. B., Downing, R., Durzi, T., Murphy, M., & Parker, V. (2021). 2021 AAHA nutrition and weight management guidelines for dogs and cats. *Journal of the American Animal Hospital Association, 57*(4), 153–178. doi: 10.5326/JAAHA-MS-7232
11. Bland, I. M., Guthrie-Jones, A., Taylor, R. D. & Hill, J. (2010). Dog obesity: Veterinary practices' and owners' opinions on cause and management. *Preventive Veterinary Medicine, 94*(3-4), 310–315. doi: 10.1016/j.prevetmed.2010.01.013
12. Porsani, M. Y. H., Teixeira, F. A., Amaral, A. R., Pedrinelli, V., Vasques, V., de Oliveira, A. G., Vendramini, T. H. A., & Brunetto, M. A. (2020). Factors associated with failure of dog's weight loss programmes. *Veterinary Medicine and Science, 6*(3), 299–305. doi: 10.1002/vms3.229
13. Levine, D. M., Savarimuthu, S., Squires, A., Nicholson, J. & Jay, M. (2015). Technology-assisted weight loss interventions in primary care: A systematic review. *Journal of General Internal Medicine, 30*(1), 107–117. doi: 10.1007/s11606-014-2987-6
14. Khaylis, A., Yiaslas, T., Bergstrom, J. & Gore-Felton, C. (2010). A review of efficacious technology-based weight-loss interventions: Five key components. *Telemedicine Journal and E-Health, 16*(9), 931–938. doi: 10.1089/tmj.2010.0065

15. Colpoys, J. & DeCock, D. (2021). Evaluation of the FitBark activity monitor for measuring physical activity in dogs. *Animals, 11*(3), 781. doi: 10.3390/ani11030781
16. Sekhar, M., Rudinsky, A. J., Cashman, C., Parker, V. J., Kieves, N. R., Howard, J., & Winston, J. (2023). Commercially available wearable health monitor in dogs is unreliable for tracking energy intake and expenditure. *American Journal of Veterinary Research, 85*(3), 1-8. doi:10.2460/ajvr.23.10.0242
17. Winston, J. A., Lenis, H., Nealon, N. J., Rudinsky, A., Klein, H., & Parker, V. (2024). Utility of FitBark to monitor activity in obese dogs undergoing a structured weight loss program (Abstract NM04). 2024 ACVIM Forum Research Abstract Program. Available in *Journal of Veterinary Internal Medicine, 38*(5), 2941-2942. doi: 10.1111/jvim.17182
18. Winston, J. A. (2023). Harnessing the power of microbes to fight obesity. 2023 ACVIM Forum, Philadelphia, Pennsylvania, June 15-17, 2023.
19. Witzel-Rollins, A., Murphy, M., Springer, C. M., Moyers, T. D., & Albright, J. D. (2022). Evaluation of a pet-separating automatic feeder and high-frequency meal feeding for weight loss in multi-cat households. *Journal of Feline Medicine and Surgery, 24*(8), e281–e288. doi: 10.1177/1098612X221105046
20. Hadar, B. N., Lambrecht, K. J., Poljak, Z., Coe, J. B., Stone, E. A., Verbrugghe, A., & Bernardo, T. M. (2022). Technology-enhanced weight-loss program in multiple-cat households: A randomized controlled trial. *Journal of Feline Medicine and Surgery, 24*(8), 726–738. doi: 10.1177/1098612X211044412

Applying -Omics Approaches, Bioinformatics, and Machine Learning to Study the Companion Animal Microbiome

Nicholas Griffin, PhD
Nestlé Purina, MO, USA
nicholas.griffin@rd.nestle.com

Glossary of Abbreviations

BCAAs	branch chain amino acids
SCFAs	short chain fatty acids
NAFLD	nonalcoholic fatty liver disease
PCR	polymerase chain reaction
16S rRNA genes	genes encoding small subunit of prokaryotic ribosomal ribonucleic acid (also called 16S rDNA)
ML	machine learning
MAG	metagenome-assembled genomes
sPLS-DA	sparse partial least squares discriminant analysis
OGTT	oral glucose tolerance test
ASV	amplicon sequence variant

Introduction

Animal health is intricately linked to interactions with the microbial communities they host. Referred to as "microbiota," these communities consist of bacteria, archaea, fungi, protists, microalgae, and even viruses, and often form recognizably distinct compositions of species across different body sites.[1] The combination of microbiota and their "theatre of activity" – the combination of these organisms, their genomes, genetic transcripts, proteins and chemical products, the features of their habitat, and their interactions between with their habitat and host – is known as a "microbiome."[1,2] Recent advances in biochemistry, computation, bioinformatics, culturomics, and machine learning (ML) enable researchers to study animal microbiomes in situ with meta-omics approaches to identify targets for nutritional interventions, develop new biotic solutions, and understand the associations between microbes and host health.[3,4,5]

How Do Microbiomes Influence Health?

Microbiomes play many roles within their animal hosts, both locally in the body sites they inhabit and systemically through their metabolites and microbe-host interactions.[6] The highly diverse and numerous organisms of the gut microbiome degrade dietary components otherwise resistant to host digestion, such as complex carbohydrates.[7] Microbially-derived short chain fatty acids serve as key energy sources for cells in the gut.[8,9] Gut microbes influence the structure of the intestinal mucus layer,[10] influence gut motility[11], inhibit colonization by pathogens[12], and interact directly with the vast array of immune cells in the gut, influencing both innate and adaptive immunity.[13] Additionally, by producing bioactive compounds that circulate systemically, or by interacting with host cells to stimulate systemic responses, gut microbes influence health across a range of physiological systems.[14,15]

Meta-omics Methods Used to Study Microbiomes

Traditional microbiology relies heavily on the ability to isolate and culture micro-organisms. In the 1990's, the observation that only a small fraction of the world's microbial diversity was cultured, combined with advances in molecular biology and DNA sequencing, led to the beginning of the meta-omics era through the adoption of 16S rRNA gene sequencing.[16] DNA could be isolated from an environmental sample, the genes encoding the 16S subunit of ribosomal rRNA could be amplified by PCR, and the resulting amplified sequences could be compared to those from known isolates. Further advances in biochemistry, microbiology, bioinformatics, and computing have since led to the development of more meta-omics strategies for studying the microbiome, including whole-genome shotgun metagenomics, metatranscriptomics, metabolomics, and metaproteomics.[3,5]

Meta-omics techniques characterize the microbiome, its environment, or its products by measuring specific categories of molecules, such as DNA, RNA, metabolites or proteins (***Table 1***).[3,5] The prefix "meta" signifies that the specific molecules are being measured as a whole (e.g., all the genomes present in the community). These methods provide the opportunity to characterize the composition, environment, and metabolic activity of microbial communities *in situ*, independent of the need to isolate and culture organisms.

Table 1: Descriptions of different meta-omics fields

Meta-omics field	Description
16S rRNA gene sequencing (metagenomics)	Identifies and quantifies bacteria and archaea and quantifies their relative proportions in an environmental sample by sequencing PCR-amplified copies of hypervariable regions of the 16S rRNA gene and comparing to reference databases.[16]
Whole genome shotgun metagenomics	Studies all the DNA in an environmental sample. Can be used to identify and quantify microorganisms, genes, genetic pathways, and to build metagenome-assembled genomes (MAGs).[17]
Metatranscriptomics	Studies gene expression from all the mRNA in an environmental sample.[18]
Metabolomics	Studies the microbiome's environment and metabolism by identifying and quantifying measurable molecules from an environmental sample. May be targeted on untargeted. Includes subcategories of specific metabolite classes (e.g., lipidomics).[19]
Metaproteomics	Studies the environment and activity by measuring the proteins present in an environmental sample.[20]
Culturomics	Methods to isolate, culture, and identify diverse organisms from a microbiome.[21]

Bioinformatics refers to the interdisciplinary field focused on interpreting biological data, including algorithms to convert the highly complex data produced by omics technologies into analyzable measures. For instance, bioinformatic pipelines are used to quantify the relative abundances of bacterial species from the frequencies of known marker genes recovered in whole genome metagenomics data.[22]

The Application of Machine Learning in Microbiome Research

Machine learning (ML) algorithms "learn" generalizable patterns from training datasets to make predictions from future data.[23] These algorithms play important roles in many aspects of meta-omics and microbiome research, from data generation and processing all the way to data analysis.

One common use of ML algorithms is to create models that use microbiome features from metagenomics, metabolomics, or metaproteomics data to predict disease states. The model is trained on a subset of the data including both healthy and diseased individuals, and then the success of its predictive ability is determined using a separate group of individuals. Finally, the most important features contributing to the model's predictive success are identified. For example, Innocente et al. created models using two different algorithms (random forest classification and sPLS-DA) to demonstrate that the relative abundances of bacterial species could predict whether a dog suffered from chronic enteropathy.[24] The authors then combined the selected taxa from each model with results from statistical models to identify taxa of interest.

Similar models have also been used to show the ability of microbial features to predict physiological responses to dietary interventions. Korem et al. observed that several clinical measures, including glycemic response, were highly variable and did not exhibit consistent differences between people fed commercial white bread or homemade sourdough bread for week-long periods.[25] However, an ML algorithm using the relative abundances of bacterial species, genes and genetic pathways at the beginning of the experiment was able to predict whether an individual would have a better glycemic response to the sourdough bread or the white bread.

In regression problems, ML algorithms are trained to predict continuous outcomes, such as an individual's age. Moreover, ML algorithms can be trained using multiple data modalities derived from different technologies. Seo et al. generated age-predictive models in 568 South Koreans from 20 to 80 years old.[26] A model based only on the relative abundances of microbes from 16S rRNA sequencing data had a mean absolute error of 5.48 years. However, combining those data with quantifications of urine metabolites produced a more accurate model with a mean absolute error of only 4.93 years.

For some ML algorithms, the decisions made by the model are difficult to interpret, including the reasons for selecting features and the specific combinations of values that lead to a particular prediction. Strategies to overcome this include exploring the relationships between features and outcomes with descriptive statistical approaches and selecting more interpretable algorithms. Gou et al. created a microbiome risk score for type 2 diabetes based on the features selected by an ML algorithm trained and tested in multiple cohorts of Chinese adults.[27] One-unit changes in the risk score led to 1.12-1.28 risk ratios in the examined test cohorts. Similarly, AlShawaqfeh et al. used ML algorithms to identify a set of predictive quantitative PCR reactions and design a predictive model for canine enteropathy, developing the canine dysbiosis index.[28]

In addition to predicting aspects of host health based on microbiome features, ML algorithms play roles in data generation and processing. For instance, assigning taxonomic information to 16S rRNA gene sequences is often performed using a machine learning classification algorithm developed by the Ribosomal Database Project,[29] and mass-spectrometry-based omics approaches utilize ML algorithms to pre-process spectra and predict molecular structures.[30] The combination of ML, omics pipelines, and automation is also fueling advances in efforts to isolate and culture microbes. Huang et al. developed a framework for performing culturomics by automated microbiome imaging and isolation (CAMII), in which an imaging system coupled to a robot performs microbial colony picking based on the predictions of an algorithm using bacterial colony morphology features as inputs.[31] In a trial of the system in 20 individuals, nearly 27,000 isolates making up 394 16S rRNA amplicon sequence variants were recovered.

Conclusion

The combination of advances in meta-omics, bioinformatics and machine learning have provided necessary tools to study the microbiome in situ and to elucidate its importance in the health and development of animals. Further advances in culturomics, including the incorporation of automation with rapid ML algorithms and omics pipelines will generate future opportunities to identify and recover microbes of interest and combine traditional microbiology and omics approaches.

Conflicts of Interest

NG is an employee of Nestlé Purina.

References

1. Berg, G., Rybakova, D., Fischer, D., Cernava, T., Verges, M. C., Charles, T., Chen, X., . . . Schloter, M. (2020). Microbiome definition re-visited: old concepts and new challenges. *Microbiome*, *8*(1), 103. doi: 10.1186/s40168-020-00875-0
2. Whipps, J., Lewis, K., & Cooke, R. (1988). Mycoparasitism and plant disease control. In M. Burge (Ed.), *Fungi in Biological Control Systems* (pp. 161-187). Manchester University Press. doi:
3. Muller, E. E., Glaab, E., May, P., Vlassis, N., & Wilmes, P. (2013). Condensing the omics fog of microbial communities. *Trends in Microbiology*, *21*(7), 325-333. doi: 10.1016/j.tim.2013.04.009
4. Sudhakar, P., Machiels, K., Verstockt, B., Korcsmaros, T., & Vermeire, S. (2021). Computational biology and machine learning approaches to understand mechanistic microbiome-host interactions. *Frontiers in Microbiology*, *12*, 618856. doi: 10.3389/fmicb.2021.618856
5. Roume, H., Heintz-Buschart, A., Muller, E. E. L., May, P., Satagopam, V. P., Laczny, C. C., Narayanasamy, S., . . . Wilmes, P. (2015). Comparative integrated omics: identification of key functionalities in microbial community-wide metabolic networks. *NPJ Biofilms and Microbiomes*, *1*, 15007. doi: 10.1038/npjbiofilms.2015.7
6. Lynch, S. V., & Pedersen, O. (2016). The human intestinal microbiome in health and disease. *New England Journal of Medicine*, *375*(24), 2369-2379. doi: 10.1056/NEJMra1600266
7. Wong, J. M., & Jenkins, D. J. (2007). Carbohydrate digestibility and metabolic effects. *Journal of Nutrition*, *137*(11 Suppl), 2539S-2546S. doi: 10.1093/jn/137.11.2539S
8. Hodgkinson, K., El Abbar, F., Dobranowski, P., Manoogian, J., Butcher, J., Figeys, D., Mack, D., & Stintzi, A. (2023). Butyrate's role in human health and the current progress towards its clinical application to treat gastrointestinal disease. *Clinical Nutrition*, *42*(2), 61-75. doi: 10.1016/j.clnu.2022.10.024
9. Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Backhed, F. (2016). From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. *Cell*, *165*(6), 1332-1345. doi: 10.1016/j.cell.2016.05.041
10. Schroeder, B. O. (2019). Fight them or feed them: how the intestinal mucus layer manages the gut microbiota. *Gastroenterology Report (Oxford)*, *7*(1), 3-12. doi: 10.1093/gastro/goy052
11. Soret, R., Chevalier, J., De Coppet, P., Poupeau, G., Derkinderen, P., Segain, J. P., & Neunlist, M. (2010). Short-chain fatty acids regulate the enteric neurons and control gastrointestinal motility in rats. *Gastroenterology*, *138*(5), 1772-1782. doi: 10.1053/j.gastro.2010.01.053
12. Stecher, B., & Hardt, W. D. (2011). Mechanisms controlling pathogen colonization of the gut. *Current Opinion in Microbiology*, *14*(1), 82-91. doi: 10.1016/j.mib.2010.10.003
13. Zheng, D., Liwinski, T., & Elinav, E. (2020). Interaction between microbiota and immunity in health and disease. *Cell Research*, *30*(6), 492-506. doi: 10.1038/s41422-020-0332-7
14. Fukasawa, N., Tsunoda, J., Sunaga, S., Kiyohara, H., Nakamoto, N., Teratani, T., Mikami, Y., & Kanai, T. (2025). The gut-organ axis: Clinical aspects and immune mechanisms. *Allergology International*, *74*(2), 197-209. doi: 10.1016/j.alit.2025.01.004
15. Bui, T. V. A., Hwangbo, H., Lai, Y., Hong, S. B., Choi, Y. J., Park, H. J., & Ban, K. (2023). The gut-heart axis: Updated review for the roles of microbiome in cardiovascular health. *Korean Circulation Journal*, *53*(8), 499-518. doi: 10.4070/kcj.2023.0048
16. Amann, R. I., Ludwig, W., & Schleifer, K. H. (1995). Phylogenetic identification and in situ detection of individual microbial cells without cultivation. *Microbiological Reviews*, *59*(1), 143-169. doi: 10.1128/mr.59.1.143-169.1995
17. Perez-Cobas, A. E., Gomez-Valero, L., & Buchrieser, C. (2020). Metagenomic approaches in microbial ecology: an update on whole-genome and marker gene sequencing analyses. *Microbial Genomics*, *6*(8). doi: 10.1099/mgen.0.000409

18. Filiatrault, M. J. (2011). Progress in prokaryotic transcriptomics. *Current Opinion in Microbiology*, *14*(5), 579-586. doi: 10.1016/j.mib.2011.07.023

19. Bauermeister, A., Mannochio-Russo, H., Costa-Lotufo, L. V., Jarmusch, A. K., & Dorrestein, P. C. (2022). Mass spectrometry-based metabolomics in microbiome investigations. *Nature Reviews Microbiology*, *20*(3), 143-160. doi: 10.1038/s41579-021-00621-9

20. Heintz-Buschart, A., & Wilmes, P. (2018). Human Gut Microbiome: Function Matters. *Trends in Microbiology*, *26*(7), 563-574. doi: 10.1016/j.tim.2017.11.002

21. Lagier, J. C., Armougom, F., Million, M., Hugon, P., Pagnier, I., Robert, C., Bittar, F., …Raoult, D. (2012). Microbial culturomics: paradigm shift in the human gut microbiome study. *Clinical Microbiology and Infection*, *18*(12), 1185-1193. doi: 10.1111/1469-0691.12023

22. Blanco-Miguez, A., Beghini, F., Cumbo, F., McIver, L. J., Thompson, K. N., Zolfo, M., Manghi, P., . . . Segata, N. (2023). Extending and improving metagenomic taxonomic profiling with uncharacterized species using MetaPhlAn 4. *Nature Biotechnology*, *41*(11), 1633-1644. doi: 10.1038/s41587-023-01688-w

23. Hernandez Medina, R., Kutuzova, S., Nielsen, K. N., Johansen, J., Hansen, L. H., Nielsen, M., & Rasmussen, S. (2022). Machine learning and deep learning applications in microbiome research. *ISME Communications*, *2*(1), 98. doi: 10.1038/s43705-022-00182-9

24. Innocente, G., Patuzzi, I., Furlanello, T., Di Camillo, B., Bargelloni, L., Giron, M. C., Facchin, S., …Simionati, B. (2022). Machine learning and canine chronic enteropathies: A new approach to investigate FMT effects. *Veterinary Science*, *9*(9). doi: 10.3390/vetsci9090502

25. Korem, T., Zeevi, D., Zmora, N., Weissbrod, O., Bar, N., Lotan-Pompan, M., Avnit-Sagi, T., …Segal, E. (2017). Bread affects clinical parameters and induces gut microbiome-associated personal glycemic responses. *Cell Metabolism*, *25*(6), 1243-1253 e1245. doi: 10.1016/j.cmet.2017.05.002

26. Seo, S. H., Na, C. S., Park, S. E., Kim, E. J., Kim, W. S., Park, C., Oh, S., …Son, H. S. (2023). Machine learning model for predicting age in healthy individuals using age-related gut microbes and urine metabolites. *Gut Microbes*, *15*(1), 2226915. doi: 10.1080/19490976.2023.2226915

27. Gou, W., Ling, C.-W., He, Y., Jiang, Z., Fu, Y., Fengzhe, X., Miao, Z.-L., …Zheng, J.-S. (2020). Interpretable machine learning algorithm reveals novel gut microbiome features in predicting Type 2 diabetes. *Current Developments in Nutrition*, *4*, 1559. doi: 10.1093/cdn/nzaa062_016

28. AlShawaqfeh, M. K., Wajid, B., Minamoto, Y., Markel, M., Lidbury, J. A., Steiner, J. M., Serpedin, E., & Suchodolski, J. S. (2017). A dysbiosis index to assess microbial changes in fecal samples of dogs with chronic inflammatory enteropathy. *FEMS Microbiology Ecoogyl*, *93*(11). doi: 10.1093/femsec/fix136

29. Wang, Q., Garrity, G. M., Tiedje, J. M., & Cole, J. R. (2007). Naive Bayesian classifier for rapid assignment of rRNA sequences into the new bacterial taxonomy. *Applied and Environmental Microbiology*, *73*(16), 5261-5267. doi: 10.1128/AEM.00062-07

30. Beck, A. G., Muhoberac, M., Randolph, C. E., Beveridge, C. H., Wijewardhane, P. R., Kenttamaa, H. I., & Chopra, G. (2024). Recent developments in machine learning for mass spectrometry. *ACS Measurement Science Au*, *4*(3), 233-246. doi: 10.1021/acsmeasuresciau.3c00060

31. Huang, Y., Sheth, R. U., Zhao, S., Cohen, L. A., Dabaghi, K., Moody, T., Sun, Y., Ricaurte, D., Richardson, M., Velez-Cortes, F., Blazejewski, T., Kaufman, A., Ronda, C., & Wang, H. H. (2023). High-throughput microbial culturomics using automation and machine learning. *Nature Biotechnology*, *41*(10), 1424-1433. doi: 10.1038/s41587-023-01674-2

Development and Practical Use of Litter Box Monitoring Devices for Feline Urinary Health and Disease (Part 1 of 3)

Ragen T.S. McGowan, PhD
Nestlé Purina PetCare, St. Louis, MO, USA
Ragen.Trudelle-SchwarzMcGowan@rd.nestle.com

Glossary of Abbreviations

AI artificial intelligence
IoT Internet of Things
ML machine learning
RFE Recursive Feature Elimination
VIF Variance Inflation Factor

Introduction: Why Build a Litter Box Monitor?

Despite being something that is often tucked away, the litter box really is a window into what is going on with a cat in terms of their health and wellbeing. Fluctuations in feline elimination behavior can indicate changes in emotional wellbeing, cat social dynamics in multi-cat households and/or changes in health. Even latent or early signs of many common health problems in cats can manifest as changes in elimination behavior. Disorders resulting in altered elimination patterns are encountered frequently in feline practice.[1,2,3] Kidney and lower urinary tract diseases are among the leading reasons that cat owners seek veterinary care. Identifying renal, urinary, or digestive conditions in cats requires quantifying clinical signs, but veterinarians face challenges due to limited access to information about a cat's elimination behavior. Typically, cats are seen only once a year for check-ups or when symptoms are severe, limiting veterinarians' datapoints. Pet owners often cannot accurately monitor their cats' elimination behaviors due to factors such as secluded litter box placement and the crepuscular habits of cats themselves. Cats are great at masking pain and discomfort and subtle cues in the form of change in behavior or output in the litter box often go unnoticed even by the most attentive pet parents.

Visual cues from litter box use can indicate health issues, but these signs may be subtle and occur in later disease stages. Many pet owners lack the knowledge to connect litter box behavior with health problems. Video recording systems[4] or journaling efforts[5] can significantly enhance the tracking of elimination events, however these methods are often seen as invasive or too cumbersome for pet owners to manage long term. To address these limitations we developed a smart litter box monitor leveraging Artificial Intelligence (AI) technology to automatically track and interpret feline weight and elimination behavior. With the progress of digital technology and the rise of the Internet of Things (IoT), various industries are increasingly adopting connected devices equipped with AI to gather and monitor data over time, and pet care is no exception. These tools can play a vital role in our efforts to provide the best possible care for our pets.

Generating "Truth Data": Letting Cats be Cats

We set out to design a digital tool that could automatically monitor the weight and elimination patterns of cats and track changes in these patterns over time. We started by developing a platform equipped with sensors that could slip seamlessly under a cat's existing litter box without requiring changes to the cat's litter box set-up. This was critical for our data collection as we know that changes in a cat's litter box environment can be a source of stress for cats. We also wanted to ensure that this data collection tool had a low profile so as to not pose a barrier for litter box entry even for senior cats with more limited mobility. We deployed these data collection platforms together with video cameras (to use as a source of "truth data" to record all interactions that the cats and their caretakers had with the litter box) into a wide variety of settings including both single and multi-cat scenarios.

The key to impactful, insightful AI is the provision of high-quality data to fuel the training of models during AI development. We collected data from over 300,000 litter box events cross-referencing the sensor data with video recordings of each event to create a robust dataset that was then used to develop algorithms to detect and track specific interactions with the litter box. In short, we collected the sensor data streaming directly from the platform under the litter box in time series with video footage from each event. The videos were then analyzed by a team of trained video labelers to identify the context of the recorded event (e.g., Was it a cat? Which cat? What was the cat doing? Was it a human? What was the human doing?), the start and stop of time of each event, and a detailed account of the specific behaviors occurring (e.g., digging, urinating, covering, scooping, adding litter). This labelled truth data was then synchronized with the raw sensor data, enabling us to develop the AI to automatically translate the sensor data into insights about the associated behavior.

Building the AI: Complicated Math Leads to Fruitful Models

Using machine learning (ML) modeling techniques we developed the capability to identify individual cats (even from a multi-cat household), track their frequency of visits to the litter box, classify those visits as a non-elimination or an elimination visit and, within elimination visits, determine if a urination or a defecation occurred. We also developed the capability to track the duration of these events and time of day patterns for specific litter box interactions. The system also measures cat weights for each visit where the cat fully enters the litter box so we can track weight fluctuations over time. The AI models were developed using a feature generation module that allowed for the extraction of common features from the load cell time series of an event. The event was then split into predetermined phases of elimination, as defined by previous research on cat elimination behavior.[6] Features were built for the whole event and each phase to capture key characteristics of the timeseries, enabling the AI model to learn better from the samples shown for training. The extracted features were inputted into different machine learning models (Weight, EventType, EliminationType, CatID, and ProperSetup) and feature selection techniques (Variance Inflation Factor (VIF)[7] and Recursive Feature Elimination (RFE)[8]) were used to identify the best performing models.

Several core AI models were developed to enable tracking of the weight and elimination patterns of individual cats:

- **Weight Model**: This model predicts the weight of a cat within +/- 100 grams. It uses load cell data to identify stable parts of the data and calculate the weight estimate.
- **EventType Model**: This multi-label model distinguishes Cat Events from Non-Cat Events. It includes classes like Cat In Box, Cat Outside Box, Partial Cat in Box, Human Scooping, and more.
- **EliminationType Model**: This model predicts the type of elimination among non-elimination, urination, defecation, and combo events.
- **CatID Model**: This model identifies unique cats in multi-cat households using weight-based and feature-based machine learning algorithms.
- **ProperSetup Model**: This model detects if the device is set up properly (stable data) or not (wobbly data) to optimize performance.

For the classification models (EventType, EliminationType, IsCat, ProperSetup), recall, precision, and/or F1 scores were used to determine the best performing models. Recall refers to the proportion of true positive predictions out of all actual positives. Precision refers to the proportion of true positive predictions out of all positive predictions (the actual values obtained via video truth labels). F1 score is a metric that combines precision and recall giving an overall metric of model performance, where F1 scores have a maximum value of 100% (indicating a perfect model), and a target threshold of above 80% was set for all classes of interest. All of the developed AI models exceed the basic 80% performance threshold metric, validating the use of load cell event data to differentiate a cat event from a human event.

Within cat events, the AI identifies if a cat fully entered the box (EventType), which cat visited the box (CatID), how much that cat weighed (Weight), what they did during the event (EliminationType), and for how long they did it. The Weight Model accurately predicts the weight of a cat within +/- 100 grams, establishing high-confidence prediction with an assumed device variance of +/- 100 grams. This means we have high confidence in the ability of the monitor to track weight gain/loss for cats over time. The CatID model was developed to identify unique cats in multi-cat households. A multi-model approach using weight-based ML algorithms and feature-based ML models was employed. Feature-based models synthesized behavioral features to capture a cat's signature "pawprint." The CatID model performs well, but cats do change over time, so the system requires periodic labeling of cat events (identifying which cat was actually in the box) to maintain model performance, especially in households with high weight overlap between the resident cats. As with any measuring device, data quality is tied to proper setup so we developed a model to identify when adjustments to monitor placement (e.g., being on a level surface, not getting hung up against a wall) are required. The ProperSetup Model optimizes performance by alerting users to setup issues and requesting action by pet owners to ensure data accuracy. The EventType Model and EliminationType Model transform the device from a smart scale into an advanced technology that provides insights into cat elimination behavior. The EliminationType Model has a weighted precision, recall, and F1 Score above 90%, indicating that the model makes correct predictions 9 out of 10 times. The EventType Model performs very well for events captured inside the litter box, but as you can imagine, sometimes confuses Cat Outside Box events due to the inherent variety of behaviors cats do around the litter box (e.g., rubbing the sides of the litter box, pawing the outside of the litter box, playing with toys near the litter box, etc.) and accidental human events (e.g., bumping into the litter box with one's foot). Future efforts to build out reliable micro litter box and elimination behavior classes may mitigate these sensor limitations.

Conclusion: A Sophisticated Tool

The smart litter box monitor described herein uses AI to learn each cat's unique litter box patterns and identify subtle but meaningful changes in weight, frequency, waste type and elimination schedule. These changes are often overlooked by cat owners, but can be early signs of health conditions requiring veterinary diagnosis. When a cat presents with possible signs for renal, urinary, endocrine or digestive diseases veterinarians are encouraged to get information about: 1) the duration and progression of clinical signs, 2) whether the episode was the patient's first or a recurrence, 3) interval between episodes and 4) presence of systemic signs (e.g., weight loss). The smart litter box monitoring system we have developed provides exactly this type of data. For apparently healthy cats, the same data for litter box use patterns can be used to track fluctuations related to emotional wellbeing or satisfaction with the litter box environment. The smart litter box monitor leverages AI technology that meets or exceeds the 80% target for performance, to track and interpret feline elimination behavior, providing comprehensive documentation of feline elimination patterns of pet cats in their home environments. It has utility as a digital tool to move us from a reactive to a proactive approach to health and wellbeing for cats.

Conflicts of Interest

The author is an employee of Nestlé Purina who funded the research and development described within.

References

1. Lund, E.M., Armstrong, P.J., Kirk, C.A., Kolar, L.M., & Klausnor, J.S. (1999). Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. *Journal-American Veterinary Medical Association*, *214*(9), 1336-1341.
2. O'Neil, D.G., Church, D.B., McGreevy, P.D., Thomson, P.C., & Brodbelt, D.C. (2014). Prevalence of disorders recorded in cats attending primary-care veterinary practices in England. *The Veterinary Journal*, *202*(2), 286-291. doi: 10.1016/j.tvjl.2014.08.004
3. Dotsenko, R., Vashchyk, Y., Zakhariev, A., Zemlianskyi, A., Seliukova, N., Gliebova, K., & Kostyshy L.M. (2022). Prevalence of internal diseases of dogs and cats: a retrospective analysis (1994-2014). *ScienceRise: Biological Science, 2*(31), 8-12. doi: 10.15587/2519-8025.2022.260493
4. Dulaney, D.R., Hopfensperger, M., Malinowski, R., Hauptman, J., & Kruger, J.M. (2017). Quantification of urine elimination behaviors in cats with a video recording system. *Journal of Veterinary Internal Medicine, 31*(2), 486-491. doi: 10.1111/jvim.14680
5. Jones, S.E., Quimby, J.M., Summers, S.C., Adams, S.M., Caney, S.M., & Rudinsky, A.J. (2022). Survey of defecation habits in apparently healthy and chronic kidney disease cats. *Journal of Feline Medical Surgery, 24*(2), 131-141. doi: 10.1177/1098612X211012684
6. McGowan, R.T.S., Ellis, J.J., Bensky, M.K., & Martin, F. (2017). The ins and outs of the litter box: A detailed ethogram of cat elimination behavior in two contrasting environments. *Applied Animal Behaviour Science, 194*, 67-78. doi: 10.1016/j.applanim.2017.05.009
7. Rawlings J. O. (1998). *Applied Regression Analysis*. Pacific Grove, CA: Duxbury Press.
8. Misra P., & Yadav A. S. (2020). Improving the classification accuracy using Recursive Feature Elimination with cross-validation. *International Journal on Emerging Technologies*, *11*, 659.

Development and Practical Use of Litter Box Monitoring Devices for Feline Urinary Health and Disease (Part 2 of 3)

Jessica Quimby, DVM, PhD, DACVIM
The Ohio State University, Columbus, OH
Quimby.19@osu.edu

Glossary of Abbreviations

CKD Chronic Kidney Disease

Utility in Chronic Kidney Disease

Litter box monitoring devices may also be particularly helpful in the management of feline chronic kidney disease (CKD) as they monitor not only weight but also urinary and fecal output. In this session, the importance of monitoring defecation frequency will specifically be addressed. In multiple species, a growing body of research supports the concept that there is significant connection between the gut and the kidney,[1] and that both systems have important influences upon the other with potential significant clinical implications. Cats with CKD have been documented to have a fecal dysbiosis characterized by decreased fecal microbial diversity and richness as well as increased gut-derived uremic toxins, both of which have implications for gut health.[2]

Monitoring Defecation Frequency

The interactions between the gut and kidney are particularly germane to the discussion of constipation. Constipation is a common clinical scenario in feline patients, particularly those with CKD, and can lead to challenges in clinical management, poor quality of life and potentially poor outcomes. Constipation is defined as the infrequent or difficult evacuation of feces. These conditions may progress to megacolon, an abnormal dilation of the colon which is typically associated with end-stage disease and permanent loss of colonic motility. Given the potential for progression and dire consequences, exploring pathophysiology and encouraging more proactive monitoring and patient assessments has the potential to improve outcomes.

The etiology of constipation associated with CKD is likely mainly a dysfunction of water balance. As the kidney fails to provide appropriate urine concentrating ability and the patient fights with chronic subclinical dehydration, water is reabsorbed from the colon to compensate. However other factors such as hypokalemia, the use of phosphate binders, and an increase in uremic toxins may also contribute to constipation in feline CKD patients.[3-6] Additionally constipation may exacerbate production of uremic toxins due to extended fecal dwell time for protein fermentation and absorption. Human patients with CKD and constipation (defined by an abnormal Bristol Stool Score) have higher concentrations of serum uremic toxins that patients with normal fecal scores, and in experimental studies in other species showed uremic toxins have negative effects on gastrointestinal motility.[7,8] A CKD model demonstrated significant improvement in uremic toxins, creatinine and even kidney histopathology subsequent to a regimen of lactulose.[9]

Importantly, decreased defecation frequency may be challenging to detect, and the caregiver may not notice an overt problem until a crisis occurs. Litter box monitor devices may provide a helpful assessment of defecation frequency. Cats with CKD with no history of overt constipation have been observed to have a significant decrease in defecation frequency when litter box monitoring devices are used to track litter box habits.[10,11] Litter box monitors may provide the ability for early disease detection and intervention as well as monitoring response to therapy.

Patient Assessment

Clinical history is very important in the assessment of constipation. Important questions include the frequency of defecation, time spent defecating, the degree of difficulty, straining, or vomiting associated with defecation as this information may not be volunteered by the caregiver. Repeated visits to the litter box or straining may be misinterpreted as straining to urinate or vice versa. This is where litter box monitoring devices may be useful in gathering pertinent information. Character of the stool should be discussed. Location and accessibility of litter boxes as well as box hygiene is also important information to capture. Fecal pellets left around the house may also indicate trouble with defecation.

Hydration status is a crucial part of patient assessment and should be recorded in the medical record. Physical exam should include palpation of the colon and may reveal small hard feces in the descending colon with a build-up of fecal material before the pelvic inlet, or, in more severe cases, a large amount of hard fecal material in the colon. Assessment for stifle, lumbosacral or hip osteoarthritis may also be helpful as significant arthritis may affect posturing make defecation more difficult. A rectal exam should be performed when possible to rule out abnormalities and the anal glands should be assessed to ensure they are not interfering with fecal evacuation.

Minimum database is important to identifying contributing factors such as hypokalemia. Diagnostic imaging including minimally abdominal radiography +/- abdominal ultrasound is key to assessing the fecal burden, the colon and the musculoskeletal structures.[12]

Nutritional Management

Hydration is not only important for promoting appropriate stool density but it is also vital for mucin layer which promotes motility. Decreased transit time is associated with drier and harder stools due to extended time for water reabsorption.[13] Therefore addressing hydration status is the key primary component to medical management. Feeding canned food instead of dry, adding water to food, or changing viscosity of water are other ways to potentially increased water consumption. Paying special attention to water sources in the house – fresh, accessible, water fountains etc., is also key. If possible, supplementation with free water (orally or with a feeding tube) is preferred to avoid the sodium load that comes with the electrolyte solutions available for subcutaneous use. However maintaining hydration by administering subcutaneous balanced electrolyte solutions appears to anecdotally improve appetite, activity and quality of life and reduce constipation in CKD patients, although no clinical trials have been performed.[14,15] Hydration should be assessed in all patients and corrected as needed in order to facilitate the efficacy of other treatments (e.g dietary fiber and laxatives).

A combination of soluble (easily fermentable) and insoluble (poorly fermentable, bulking) is typically recommended for management of constipation, however few studies have been done in cats. Insoluble fiber adds bulk, draws water and stimulates colonic motility. Soluble, fermentable fibers are associated with production of SCFA by colonic bacteria, an important nutrient for intestinal epithelial cells.[16] However this is a generalization and not all soluble fibers are fermentable nor are all insoluble fibers unfermentable, and there is a range of fermentability for each fiber type. A psyllium-enriched diet was found to be helpful in management of feline constipation (not associated with CKD) in a previous open field trial and led to a decrease in the concurrent use of laxatives and promotility agents.[17] However, in CKD patients a renal diet would be the preferred therapeutic diet of choice, therefore fiber sources (psyllium 1-4 tsp daily) are commonly added to canned food. The efficacy of these types of fiber on the management of constipation has not been assessed in patients with CKD. In general trial and error for types of diet and fiber that might benefit an individual patient is anticipated.

Medical Management

Hypokalemia should be identified and addressed. Although the efficacy of potassium supplementation has not been evaluated in patients with constipation, potassium is necessary for both smooth and skeletal muscle function and hypokalemia has been identified as a risk factor in cats presenting for constipation.[6] A reasonable therapeutic goal is maintaining serum potassium >4 meq/L. Medical management of osteoarthritis may also be an important adjunctive treatment for constipation in elderly patients to facilitate appropriate posturing during defecation. Environmental management that includes accessible, yet private litter boxes is key. *After* correction of hydration imbalance and hypokalemia, oral osmotic stool softeners are often a major part of management of constipation. Polyethylene glycol 3350 is an osmotic that has been assessed in normal cats and found to be effective for softening stool.[18] It is commonly prescribed (1/8 – 1/4 tsp q 12-24 hrs titrated to effect) and is thought by some to be more effective than lactulose which is processed by intestinal microflora and may lead to bloating.[18] Another important consideration is that polyethylene glycol comes as a powder that appears to be well tolerated (and more likely to end up in the patient as opposed to all over it). Promotility agents are a common form of medical management for constipation. Cisapride (2.5-5 mg/cat q 8 hr) is the most common promotility medication used. Although supported by feline-specific pharmacokinetics and a demonstrated positive effect on contractility in normal and abnormal feline colonic smooth muscle *in vitro*,[19,20] it has not been assessed in clinical trials. Probiotics may be a helpful adjunctive therapy. In one uncontrolled clinical trial assessing probiotic use in medically refractory idiopathic constipation, 7/10 cats had clinical improvement in fecal consistency.[21]

Conclusion

Utilization of litter box monitors can aid in management of feline CKD. Prompt identification of constipation is key to improving outcomes. Improved monitoring to allow earlier detection of disease and gauge respond to therapy will help tailor management.

Conflicts of Interest

Dr. Quimby is on an advisory board for Gallant, Elanco, Nestle Purina PetCare, and Zoetis; receives speaker honoraria from Dechra, Elanco, Hills, Nestle Purina Petcare, and Royal Canin; and engages in consulting with Dechra, Gallant, Hills, and Zoetis. She receives research funding support from Dechra, Nestle Purina Petcare, Triviumvet, and Zoetis.

References

1. Ai, S., Li, Y., Tao, J., Zheng, H., Tian, L., Wang, Y., Wang, Z., & Liu, W. J. (2023). Bibliometric visualization analysis of gut-kidney axis from 2003 to 2022. *Frontiers in Physiology*, *14*, 1176894. doi: 10.3389/fphys.2023.1176894
2. Summers, S. C., Quimby, J. M., Isaiah, A., Suchodolski, J. S., Lunghofer, P. J., & Gustafson, D. L. (2019). The fecal microbiome and serum concentrations of indoxyl sulfate and p-cresol sulfate in cats with chronic kidney disease. *Journal of Veterinary Internal Medicine*, *33*(2), 662-669. doi: 10.1111/jvim.15389
3. Chen, J. Z., Deng, A. W., & Xu, J. F. (2005). Electroenterogram manifestations and significance in hypokalemia. *Di Yi Jun Yi Da Xue Xue Bao*, *25*(1), 7-9.
4. Kidder, A. C., & Chew, D. (2009). Treatment options for hyperphosphatemia in feline CKD: what's out there? *Journal of Feline Medicine and Surgery*, *11*(11), 913-924. doi: 10.1016/j.jfms.2009.09.012

5. Quimby, J., & Lappin, M. (2016). Evaluating sucralfate as a phosphate binder in normal cats and cats with chronic kidney disease. *Journal of the American Animal Hospital Association*, *52*(1), 8-12. doi: 10.5326/Jaaha-Ms-6213
6. Benjamin, S. E., & Drobatz, K. J. (2019). Retrospective evaluation of risk factors and treatment outcome predictors in cats presenting to the emergency room for constipation. *Journal of Feline Medicine and Surgery*, 22(2), 153-160. doi: 10.1177/1098612X19832663
7. Ramos, C. I., Armani, R. G., Canziani, M. E., Ribeiro Dolenga, C. J., Nakao, L. S., Campbell, K. L., & Cuppari, L. (2019). Bowel habits and the association with uremic toxins in non-dialysis-dependent chronic kidney disease patients. *Journal of Renal Nutrition, 30(1), 31-35*. doi: 10.1053/j.jrn.2019.02.004
8. Hoibian, E., Florens, N., Koppe, L., Vidal, H., & Soulage, C. O. (2018). Distal colon motor dysfunction in mice with chronic kidney disease: Putative role of uremic toxins. *Toxins (Basel)*, *10*(5), 204. doi: 10.3390/toxins10050204
9. Sueyoshi, M., Fukunaga, M., Mei, M., Nakajima, A., Tanaka, G., Murase, T., Narita, Y., Hirata, S., & Kadowaki, D. (2019). Effects of lactulose on renal function and gut microbiota in adenine-induced chronic kidney disease rats. *Clinical and Experimental Nephrology*, *23*(7), 908-919. doi: 10.1007/s10157-019-01727-4
10. Jones, S. E., Quimby, J. M., Summers, S. C., Adams, S. M., Caney, S. M., & Rudinsky, A. J. (2022). Survey of defecation habits in apparently healthy and chronic kidney disease cats. *Journal of Feline Medicine and Surgery*, *24*(2), 131-141. doi: 10.1177/1098612X211012684
11. George, Z., Quimby, J., Brusach, K., Lim, L., Jones, S., & Rudinsky, A. J. (2024). Comparing defecation frequency between cats with and without chronic kidney disease. ACVIM Forum, Minneapolis, MN. Abstract available in *Journal of Veterinary Internal Medicine, 38*(5), 2951-2952. doi: 10.1111/jvim.17182
12. Trevail, T., Gunn-Moore, D., Carrera, I., Courcier, E., & Sullivan, M. (2011). Radiographic diameter of the colon in normal and constipated cats and in cats with megacolon. *Veterinary Radiology and Ultrasound*, *52*(5), 516-520. doi: 10.1111/j.1740-8261.2011.01830.x
13. Ikee, R., Yano, K., & Tsuru, T. (2019). Constipation in chronic kidney disease: it is time to reconsider. *Renal Replacement Therapy*, *5*(1). doi: 10.1186/s41100-019-0246-3
14. Polzin, D. J. (2011). Chronic kidney disease in small animals. *Veterinary Clinics of North America: Small Animal Practice*, *41*(1), 15-30. doi: 10.1016/j.cvsm.2010.09.004
15. Polzin, D. J. (2013). Evidence-based step-wise approach to managing chronic kidney disease in dogs and cats [Review]. *Journal of Veterianry Emergency and Critical Care*, *23*(2), 205-215. doi: 10.1111/vec.12034
16. Moreno, A. A., Parker, V. J., Winston, J. A., & Rudinsky, A. J. (2022). Dietary fiber aids in the management of canine and feline gastrointestinal disease. *Journal of the American Veterinary Medical Association*, *260*(S3), S33-S45. doi: 10.2460/javma.22.08.0351
17. Freiche, V., Houston, D., Weese, H., Evason, M., Deswarte, G., Ettinger, G., Soulard, Y., Biourge, V., & German, A. J. (2011). Uncontrolled study assessing the impact of a psyllium-enriched extruded dry diet on faecal consistency in cats with constipation [Clinical Trial Research Support, Non-U.S. Gov't]. *Journal of Feline Medicine and Surgery*, *13*(12), 903-911. doi: 10.1016/j.jfms.2011.07.008
18. Tam, F. M., Carr, A. P., & Myers, S. L. (2011). Safety and palatability of polyethylene glycol 3350 as an oral laxative in cats [Clinical Trial Research Support, Non-U.S. Gov't]. *Journal of Feline Medicine and Surgery*, *13*(10), 694-697. doi: 10.1016/j.jfms.2011.05.017
19. LeGrange, S. N., Boothe, D. M., Herndon, S., & Willard, M. D. (1997). Pharmacokinetics and suggested oral dosing regimen of cisapride: a study in healthy cats [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Journal of the American Animal Hospital Association*, *33*(6), 517-523. doi: 10.5326/15473317-33-6-517
20. Washabau, R. J., & Sammarco, J. (1996). Effects of cisapride on feline colonic smooth muscle function [Comparative Study Research Support, Non-U.S. Gov't]. *American Journal of Veterinary Research*, *57*(4), 541-546.
21. Rossi, G., Jergens, A., Cerquetella, M., Berardi, S., Di Cicco, E., Bassotti, G., Pengo, G., & Suchodolski, J. S. (2018). Effects of a probiotic (SLAB51) on clinical and histologic variables and microbiota of cats with chronic constipation/megacolon: a pilot study. *Beneficial Microbes*, *9*(1), 101-110. doi: 10.3920/BM2017.0023

Development and Practical Use of Litter Box Monitoring Devices for Feline Urinary Health and Disease (Part 3 of 3)

Ashlie Saffire, DVM, Diplomate ABVP (feline practice)
Faithful Friends Veterinary Clinic & Cat Specialty Center, Dublin, Ohio, USA
Dr.Saffire@faithfulfriendsvc.com

Glossary of Abbreviations

LUTD	Lower urinary tract disease
LUTS	Lower urinary tract signs
FIC	Feline idiopathic cystitis
FLUTD	Feline lower urinary tract disease

Introduction

Lower urinary tract (LUT) diseases in cats can present with various clinical signs, including hematuria, stranguria, pollakiuria, dysuria, and periuria. Recently, it has been proposed to move away from the acronym "FLUTD" when describing cats with lower urinary tract signs (LUTS) as the term is not a true diagnosis, fails to accurately describe the underlying cause of clinical signs, and may lead to a premature diagnostic conclusion.[1] Instead, the verbiage **"lower urinary tract diseases"** is recommended, as it more accurately reflects the multiple potential causes of LUTS rather than suggesting a singular diagnosis.[1]

Feline idiopathic cystitis (FIC), crystalluria (20-50 crystals/hpf along with clinical signs), urolithiasis, bacterial cystitis, urethral obstruction, neoplasia, neurogenic disease and behavioral issues are all examples of feline lower urinary tract diseases, with FIC representing 55-67% of cases.[2,3] When presented with a patient experiencing LUTS, it is the responsibility of the clinician to thoroughly investigate all possible causes, each and every time. It should never be assumed that recurrent LUTS always have the same underlying cause as often they do not.[3] Physical examination, urinalysis, and imaging of the urinary tract should be considered a minimum database in order to arrive at a definitive diagnosis and execute a proper treatment plan.

Generally speaking, FIC is a diagnosis of exclusion and based on current evidence, still represents a complex systemic disorder with a lack of distinguishing signs or testing. The cause is widely accepted as a link between environmental stress, anxiety/fear, activation of the central threat response system and subsequent bladder inflammation and pain.[1,4] Often, feline patients suffering from FIC also have multiple concurrent nervous, endocrine and/or immune abnormalities present.[5] For as many as 36-61% cats, FIC is a chronic and recurrent syndrome.[4,6] especially for those cats who also experience higher levels of fear and anxiety-related problems.[4]

Management of FIC requires a combination of analgesia to address the acute pain, but also environmental modification to reduce the likelihood of activating the central threat response system and prevent reoccurrence.[1,4] In some cases FIC may lead to obstructive disease, therefore early detection and prompt intervention of clinical signs can be lifesaving. Because cats by nature hide illness and pain as a survival mechanism, FIC may become quite progressed by the time the caregiver recognizes there is a problem. This can ultimately lead to extended periods of pain, negative welfare and potentially life-threatening obstruction for the patient. Litter box monitoring devices are a useful modality when it comes to detecting subtle changes in toileting and can promptly alert the pet parent to a potential problem, such as increased frequency of trips to the litter box or failure to urinate when in the box.

Bladder neoplasia is another excellent example of a LUT disease where litter box monitoring devices may be helpful for disease management and identification of progression. The urinary bladder is the second most common site of urinary tract neoplasia in cats after renal lymphoma, with urothelial carcinoma (previously termed transitional cell carcinoma) the most common type of bladder neoplasia reported.[7,8] Over time, uncontrolled pain or progression of the tumor size will result in the development of LUTS, an inability to urinate, and changes in patient body weight. A litter box monitor will alert the caregiver to these changes, prompting them to seek veterinary care.

Urolithiasis is another important cause of LUTD in cats, making up 20-23% of all cases.[9,10] Over the past several decades, there have been changes in the composition of feline urinary tract stones. From 1985-1995, 80% of stones were reportedly struvite, however from 1995-2005 calcium oxalate became more common.[9] Possible over-acidification of commercial cat food has been a proposed reason for this shift in stone composition.[9] Since 2005 however, struvite (magnesium ammonium phosphate) has once again become more common than calcium oxalate. Today, both types make up 90-95% of all feline uroliths worldwide.[9] Urate stones follow as the next most common (~ 5%), followed by even rarer types including cystine, xanthine, silica, and blood stone.[9] Recently in the last year there have been reports of a new stone type containing antiviral compound GS-441524 used for the treatment of feline infectious peritonitis.[11]

Dissolution of struvite urolithiasis without the need for surgical intervention, and the prevention of struvite and calcium oxalate uroliths is now possible thanks to the development of diets that promote urine dilution, lower urine pH, low relative supersaturation, and alter urine mineral solute concentrations.[12] For these patients prone to urolithiasis, litter box monitoring devices can be used to assess a patient's urination habits when efforts to increase water intake are being made, and will also alert the pet parent in the event urination habits change.

Conclusion

In summary, litter box monitoring devices have the opportunity to provide excellent monitoring at home for many lower urinary tract diseases in cats. By keeping the pet parent aware of changes in toileting behaviors and body weight, better care can be provided, positively impacting feline welfare.

Conflicts of Interest

The author is the recipient of a research grant funded by Purina, however this does not cause any direct conflict of interest in relation to these proceedings.

References

1. Taylor, S., Boysen, S., Buffington T., Chalhoub, S., Defauw, P., Delgado, M. M. Gunn-Moore, D., & Korman, R. (2025). 2025 iCatCare consensus guidelines on the diagnosis and management of lower urinary tract diseases in cats. *Journal of Feline Medicine and Surgery, 27*(2), 1098612X241309176. doi: 10.1177/1098612X241309176

2. He, C., Fan, K., Hao, Z., Tang, N., Li, G., & Wang. S. (2022). Prevalence, risk factors, pathophysiology, potential biomarkers and management of feline idiopathic cystitis: An update review. *Frontiers in Veterinary Science, 9*, 900847. doi: 10.3389/fvets.2022.900847

3. Kaul, E., Hartmann, K., Reese, S., & Dorsch, R. (2020). Recurrence rate and long term course of cats with feline lower urinary tract disease. *Journal of Feline Medicine and Surgery, 22*(6), 544-556. doi: 10.1177/1098612X19862887

4. Caudron, M., Laroche, P., Bazin, I., & Desmarchelier, M. (2025). Association between behavioral factors and recurrence rate in cats with feline" idiopathic" cystitis. *Journal of Veterinary Behavior, 78*, 90-96. doi: 10.1016/j.jveb.2025.02.005

5. Westropp, J. L., Delgado, M., & Buffington, C. A. T. (2019). Chronic lower urinary tract signs in cats: current understanding of pathophysiology and management. *Veterinary Clinics of North America: Small Animal Practice, 49*(2), 187-209. doi: 10.1016/j.cvsm.2018.11.001
6. Eggertsdóttir, A. V., Blankvandsbråten, S., Gretarsson, P., Olofsson, A. E., & Lund, H. S. (2021). Retrospective interview-based long-term follow-up study of cats diagnosed with idiopathic cystitis in 2003–2009. *Journal of Feline Medicine and Surgery, 23*(10), 945-951. doi: 10.1177/1098612X21990302
7. Griffin, S. (2020). Feline abdominal ultrasonography: What's normal? What's abnormal? Renal pelvis, ureters and urinary bladder. *Journal of Feline Medicine and Surgery, 22*(9), 847-865. doi: 10.1177/1098612X20941786
8. Griffin, M. A., Culp, W. T. N., Giuffrida, M. A., Ellis, P., Tuohy, J., Perry, J. A., Gedney, A., …Kent, M. S. (2020). Lower urinary tract transitional cell carcinoma in cats: Clinical findings, treatments, and outcomes in 118 cases. *Journal of Veterinary Internal Medicine, 34*(1), 274-282. doi: 10.1111/jvim.15656
9. Kopecny, L., Palm, C. A., Segev, G., Larsen, J. A., & Westropp, J. L. (2021). Urolithiasis in cats: Evaluation of trends in urolith composition and risk factors (2005-2018). *Journal of Veterinary Internal Medicine, 35*(3), 1397-1405. doi: 10.1111/jvim.16121
10. Gerber, B., Boretti, F. S., Kley, S., Laluha, P., Müller, C., Sieber, N., Unterer, S., …Reusch, C. E. (2005). Evaluation of clinical signs and causes of lower urinary tract disease in European cats. *Journal of Small Animal Practice, 46*(12), 571-7. doi: 10.1111/j.1748-5827.2005.tb00288.x
11. Allinder, M., Tynan, B., Martin, C., Furbish, A., Austin, G., Bartges, J., & Lourenço BN. (2024). Uroliths composed of antiviral compound GS-441524 in 2 cats undergoing treatment for feline infectious peritonitis. *Journal of Veterinary Internal Medicine, 38*(1), 370-4. doi: 10.1111/jvim.16954
12. Queau. (2014). Urinary relative supersaturation and urolithiasis risk. *Veterinary Focus, 24* (1).

Multi-omics Approaches to Understanding Human Health and Disease

Michael Snyder, PhD
Department of Genetics, Standard University, Stanford, California, USA
mpsnyder@stanford.edu

Proceedings for this presentation are not yet available.

Unraveling Canine Gut Microbiome Dynamics: Insights into Maturation, Psychobiotics, and Pathogenic *Salmonella* Mitigation

Xu Wang, PhD
Associate Professor in Comparative Genomics
Department of Pathobiology, College of Veterinary Medicine, Auburn, Alabama, USA
xuwang@auburn.edu

Glossary of abbreviations

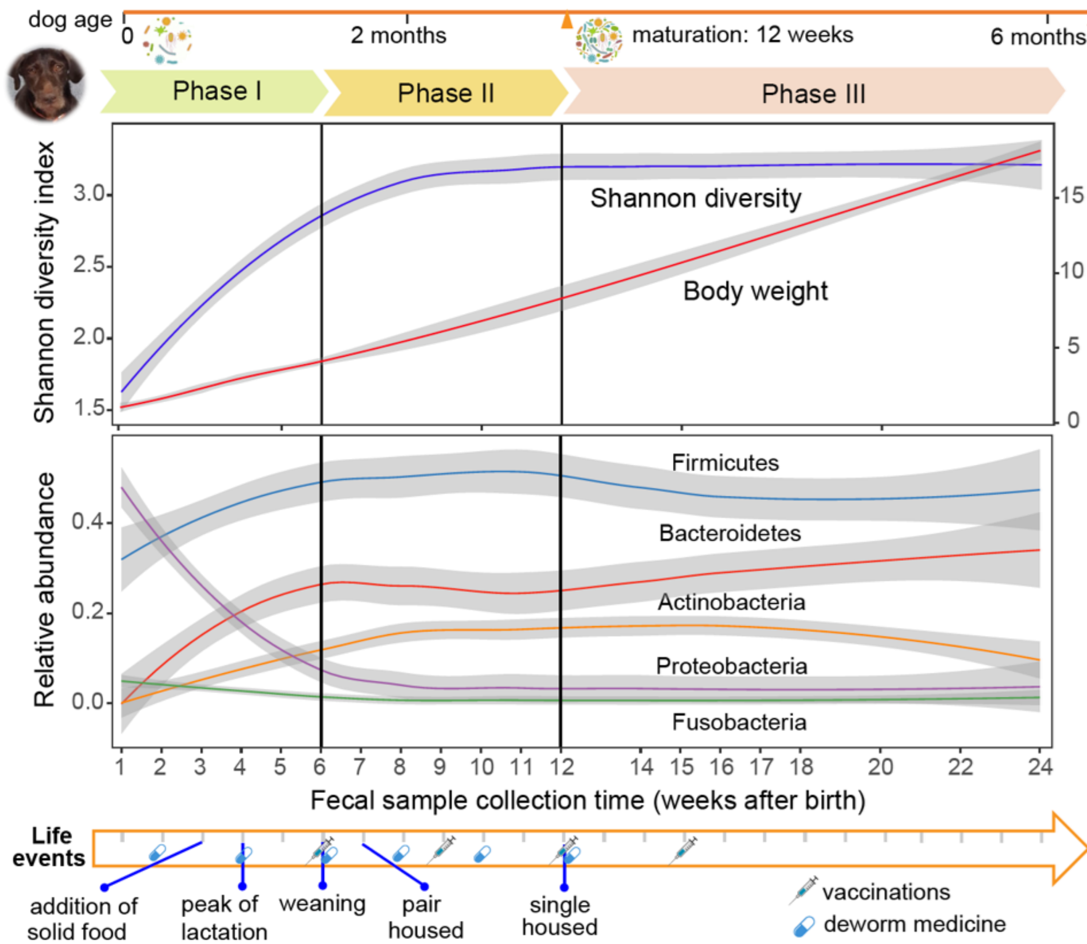
FMT	fecal microbiota transplantation
LEfSe	Linear Discriminant Analysis Effect Size
OMS	overall memory scores
PCoA	Principal Coordinates Analysis
PERMANOVA	permutational multivariate analysis of variance
WGS	whole-genome shotgun

Introduction

The gut microbiome is the entire community of microorganisms in the gastrointestinal tract,[1] which provides essential nutrients for the host and affects host metabolism, nutrition, gut health, immunity, and other aspects of host physiology.[2,3] The composition and abundance of the gut microbiome are directly influenced by diet[4] and host genetics.[5,6] Most of the gut microbiome development and maturation knowledge comes from human literature. It is now well established that infants are not born with an adult-type microbiome; rather, the gut flora undergoes a progressive transformation from a relatively simple, newly inoculated neonatal microbiome to a complex, functionally mature adult-like microbial ecosystem.[7] In contrast, our understanding of microbiome development in dogs remains limited. Only a couple of longitudinal studies have investigated the temporal dynamics, primarily relying on 16S rDNA sequencing approaches,[8,9] which offer limited taxonomic resolution and insufficient insight into functional potential.

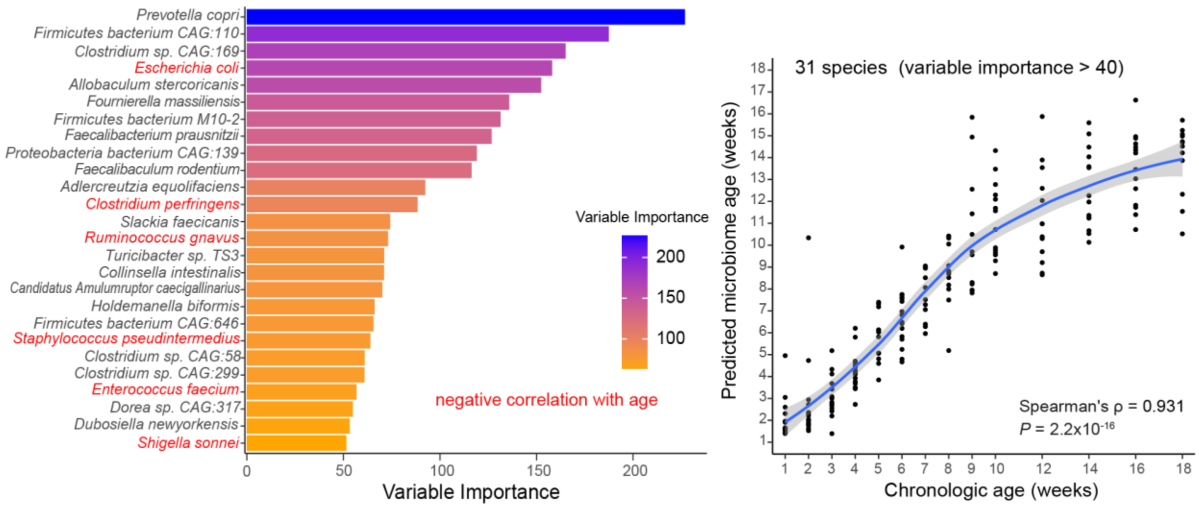
A Significant Shift in Microbiome Composition from Birth to Six Months of Age

Using WGS metagenomic sequencing, we characterized the developmental dynamics of the canine gut microbiome by analyzing 238 fecal samples collected longitudinally from 16 puppies from birth to 24 weeks of age. A total of 6 Tbp sequences were generated, with an average of over 160 million reads per sample, offering unprecedented resolution into the microbial composition and functional profile during early life. At birth, the puppy's microbiome exhibited low microbial diversity and was dominated by Proteobacteria, resembling the microbial communities found in the maternal skin and vaginal microbiome. A significant shift in phylum-level composition occurred through the peak of lactation until weaning (6 weeks), and the rank order of abundance among the 5 major phyla diverged markedly from that observed in the adult canine microbiome. We define this initial period (0~6 weeks) as Phase I, or the developmental phase, hallmarked by a linear increase in alpha diversity and significant changes in phylum-level composition. During Phase II, or transitional phase (6~12 weeks of age), microbial diversity continued to increase before reaching a plateau. While compositional changes at the phylum level persisted, the relative rank order of the 5 dominant phyla remained unchanged. By 12 weeks of age, the composition and diversity of the puppy microbiome closely resembled that of adult dogs. Therefore, we concluded that dog microbiome reaches a mature profile between 9 and 12 weeks of age in development, which roughly corresponds to 2~6.5 years of age in human infants.[10] Given that the human gut microbiome was reported to reach adult-like maturity by 3 years of age,[11] this timeline aligns well between humans and dogs.



Microbiome Age from Featured Microbial Species Predicts Chronological Age

Through unsupervised clustering analysis using the lowest Laplace approximation criterion, we identified 5 distinct clusters of microbiome profiles across 238 longitudinal samples. These clusters demonstrated clear correspondence to the three defined phases of microbiome maturation, as confirmed by PERMANOVA analysis. To further elucidate phase-specific microbial signatures, we employed Linear Discriminant Analysis Effect Size (LEfSe), which identified 31 featured species that were significantly enriched in one or more developmental stages. These featured species were subsequently utilized to construct a predictive model of microbiome age using a machine learning framework.[12] This Random Forest model exhibited a high predictive accuracy, achieving a Spearman correlation coefficient of 0.931 within 18 weeks of age. In children, persistent immaturity of the gut microbiome has been reported to be associated with malnutrition.[13] The nearly perfect correlation between predicted microbiome age and chronological age established the canine microbiome age as a potential biomarker for assessing the developmental status of the canine gut microbiome, which could be utilized to identify deviations from expected maturation trajectories, offering a powerful tool for detecting delays or disruptions in microbiome development. Such delays may result from dietary imbalances, pathogenic infections, environmental stressors, antibiotic exposure, or other perturbations during critical periods of early life. This early detection can inform potential interventions, such as the administration of prebiotics, probiotics, or fecal microbiota transplantation (FMT), to restore a healthy and mature microbiome.



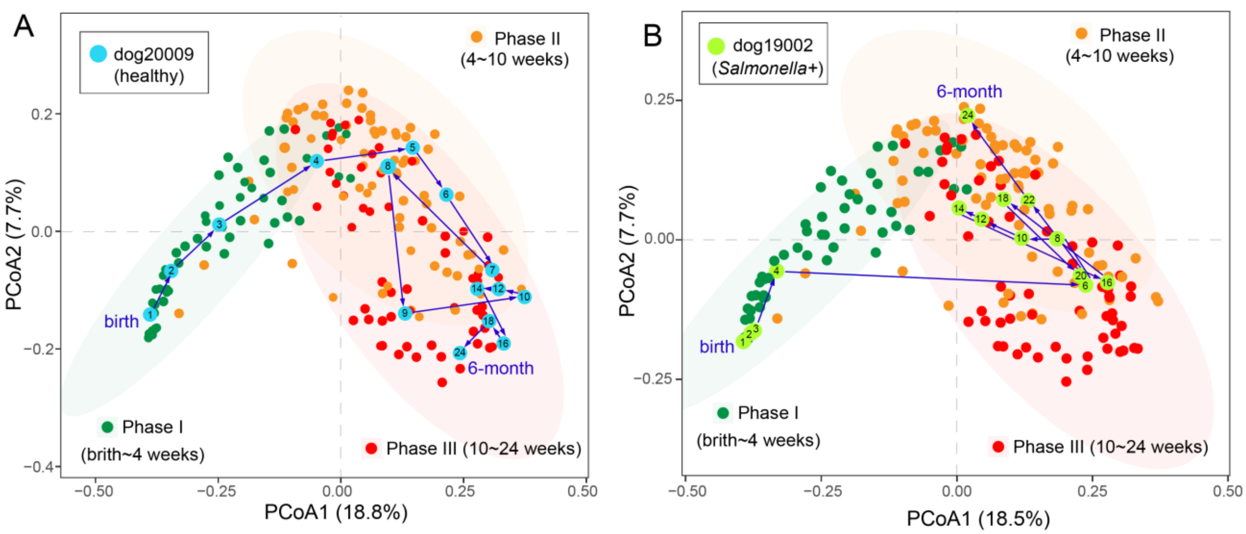
Developmental Increase of a *Bifidobacteria* Species Associated with Short-term Memory Performance

Memory has been identified as the least heritable cognitive trait in domestic dogs,[14] suggesting a substantial influence of non-genetic factors. To investigate the influence of the gut microbiome on memory performance, we assessed overall memory scores (OMS) in a cohort of 27 young dogs at three developmental timepoints (3, 6, and 12 months of age). Using a Random Forest regression model, we evaluated the predictive value of variables such as sex, litter, and breed identity, all of which demonstrated minimal importance for predicting OMS. Although a trend toward improved memory performance with age was observed, it did not achieve statistical significance. In the gut microbiome, a single bacterial species, *Bifidobacterium pseudolongum*, was identified and confirmed to be associated with elevated OMS.[15] This finding parallels human studies, in which *Bifidobacterium longum 1714* has been linked to improved memory and reduced stress via neural modulation mechanisms.[16,17] However, in our canine study, *B. longum* exhibited a 100-fold lower relative abundance compared to *B. pseudolongum* and showed no association with working memory, suggesting species-specific differences in host-microbe interactions and neurocognitive modulation. Importantly, *B. pseudolongum* is one of the 31 featured bacterial species identified as predictive markers of microbiome age. It was nearly absent in the newborn puppy microbiome and became significantly enriched during Phase III of microbiome maturation. These findings suggest a potential psychobiotic role of *B. pseudolongum* in canine neurodevelopment and cognition, supporting further investigation into its mechanistic contributions to memory in dogs.

A Natural Outbreak of Pathogenic Infections Rewinds the Puppy Microbiome Clock and Delays Microbiome Maturation

During the longitudinal microbiome study, two dogs were affected by a natural outbreak of *Salmonella* infection. Fecal samples were collected from symptomatic puppies and subjected to

WGS metagenomic sequencing for comparative microbiome analysis. Principal Coordinates Analysis (PCoA) of beta diversity, based on Bray-Curtis dissimilarity at the species level, revealed significant separation among gut microbiomes corresponding to the three defined phases of development (PERMANOVA, $P < 0.001$). Among healthy animals, individual developmental trajectories followed the expected progression through the defined phases of microbiome maturation. For example, puppy dog20009 exhibited a well-ordered transition from Phase I to Phase II to Phase III, with microbial community profiles advancing in accordance with chronological age and microbiome age predictions. In contrast, dog19002 tested positive for *Salmonella* infection between 10 and 12 weeks of age, and showed a significant delay in the development of its microbiome. The trajectory wandered around the Phase II region, failing to progress toward a stabilized adult-like composition. Notably, at 24 weeks of age, the microbiome was comparable to that of healthy 5~6-week-old puppies, as determined by microbiome age estimation. Enteric infections can severely disrupt the normal gut microbiome development in puppies, making microbiome age a useful indicator for detecting delays and necessitating early, microbiome-targeted interventions to restore healthy maturation.



Conclusion

In conclusion, our longitudinal metagenomic analysis reveals a significant and structured shift in gut microbiome composition in dogs from birth to six months of age, delineating three distinct developmental phases characterized by increasing microbial diversity and taxonomic complexity. Through machine learning approaches, we identified a panel of 31 featured microbial species whose relative abundances reliably predict chronological age, establishing microbiome age as a potential biomarker for gut microbiome maturation. Among these species, *Bifidobacterium pseudolongum* demonstrated a developmental increase in abundance during the stabilization phase and was positively associated with short-term memory performance in young dogs, suggesting a potential psychobiotic role in cognitive development. Furthermore, A natural outbreak of *Salmonella* infection provided clear evidence that pathogenic perturbations can significantly delay gut microbiome maturation. Species-level microbiome analysis facilitated accurate predictions of microbiome age, enabling a quantitative assessment of developmental delays associated with potential gut health issues. These findings revealed the importance of maintaining microbial homeostasis during early life and highlight the microbiome age as a useful indicator of gut development, supporting the need for early, targeted interventions to restore healthy microbial trajectories.

Conflicts of Interest

None.

References

1. Barko, P. C., McMichael, M. A., Swanson, K. S., & Williams, D. A. (2018). The Gastrointestinal Microbiome: A Review. *Journal of Veterinary Internal Medicine*, *32*(1), 9-25. doi: 10.1111/jvim.14875
2. Thaiss, C. A., Zmora, N., Levy, M., & Elinav, E. (2016). The microbiome and innate immunity. *Nature*, *535*(7610), 65-74. doi: 10.1038/nature18847
3. Olsthoorn, L., Vreeken, D., & Kiliaan, A. J. (2021). Gut Microbiome, Inflammation, and Cerebrovascular Function: Link Between Obesity and Cognition. *Frontiers in Neuroscience*, *15*, 761456. doi: 10.3389/fnins.2021.761456
4. Singh, R. K., Chang, H.-W., Yan, D., Lee, K. M., Ucmak, D., Wong, K., Abrouk, M., Farahnik, B., Nakamura, M., & Zhu, T. H. (2017). Influence of diet on the gut microbiome and implications for human health. *Journal of Translational Medicine*, *15*(1), 1-17. doi: 10.1186/s12967-017-1175-y
5. Grieneisen, L., Dasari, M., Gould, T. J., Bjork, J. R., Grenier, J. C., Yotova, V., Jansen, D., . . . Blekhman, R. (2021). Gut microbiome heritability is nearly universal but environmentally contingent. *Science*, *373*(6551), 181-186. doi: 10.1126/science.aba5483
6. Morris, A. H., & Bohannan, B. J. M. (2024). Estimates of microbiome heritability across hosts. *Nature Microbiology*, *9*(12), 3110-3119. doi: 10.1038/s41564-024-01865-w
7. Stewart, C. J., Ajami, N. J., O'Brien, J. L., Hutchinson, D. S., Smith, D. P., Wong, M. C., Ross, M. C., Lloyd, R. E., Doddapaneni, H., & Metcalf, G. A. (2018). Temporal development of the gut microbiome in early childhood from the TEDDY study. *Nature*, *562*(7728), 583-588. doi: 10.1038/s41586-018-0617-x
8. Guard, B. C., Mila, H., Steiner, J. M., Mariani, C., Suchodolski, J. S., & Chastant-Maillard, S. (2017). Characterization of the fecal microbiome during neonatal and early pediatric development in puppies. *PloS one*, *12*(4), e0175718. doi: 10.1371/journal.pone.0175718
9. Pereira, A. M., Pinna, C., Biagi, G., Stefanelli, C., Maia, M. R., Matos, E., Segundo, M. A., Fonseca, A. J., & Cabrita, A. R. J. (2020). Supplemental selenium source on gut health: Insights on fecal microbiome and fermentation products of growing puppies. *FEMS Microbiology Ecology*, *96*(11), fiaa212. doi: 10.1093/femsec/fiaa212
10. Wang, T., Ma, J., Hogan, A. N., Fong, S., Licon, K., Tsui, B., Kreisberg, J. F., Adams, P. D., Carvunis, A. R., Bannasch, D. L., Ostrander, E. A., & Ideker, T. (2020). Quantitative translation of dog-to-human aging by conserved remodeling of the DNA methylome. *Cell Systems*, *11*(2), 176-185 e176. doi: 10.1016/j.cels.2020.06.006
11. Sawhney, S. S., Thanert, R., Thanert, A., Hall-Moore, C., Ndao, I. M., Mahmud, B., Warner, B. B., Tarr, P. I., & Dantas, G. (2025). Gut microbiome evolution from infancy to 8 years of age. *Nature Medicine,* online ahead of print. doi: 10.1038/s41591-025-03610-0
12. Breiman, L. (2001). Random Forests. *Machine Learning*, *45*(1), 5-32. doi: 10.1023/A:1010933404324
13. Subramanian, S., Huq, S., Yatsunenko, T., Haque, R., Mahfuz, M., Alam, M. A., Benezra, A., ...Gordon, J. I. (2014). Persistent gut microbiota immaturity in malnourished Bangladeshi children. *Nature*, *510*(7505), 417-421. doi: 10.1038/nature13421
14. Gnanadesikan, G. E., Hare, B., Snyder-Mackler, N., & MacLean, E. L. (2020). Estimating the heritability of cognitive traits across dog breeds reveals highly heritable inhibitory control and communication factors. *Animal Cognition*, *23*(5), 953-964. doi: 10.1007/s10071-020-01400-4
15. Ma, X., Lazarowski, L., Zhang, Y., Krichbaum, S., Smith, J. G., Zheng, J., Cao, W., Haney, P. S., Wilborn, R. R., Price, S. B., Singletary, M., Waggoner, P., & Wang, X. (2024). Associations between memory performance and *Bifidobacterium pseudolongum* abundance in the canine gut microbiome. *iScience*, *27*(5), 109611. doi: 10.1016/j.isci.2024.109611
16. Allen, A. P., Hutch, W., Borre, Y. E., Kennedy, P. J., Temko, A., Boylan, G., Murphy, E., Cryan, J. F., Dinan, T. G., & Clarke, G. (2016). *Bifidobacterium longum* 1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. *Translational Psychiatry*, *6*(11), e939. doi: 10.1038/tp.2016.191
17. Wang, H., Braun, C., Murphy, E. F., & Enck, P. (2019). *Bifidobacterium longum* 1714 strain modulates brain activity of healthy volunteers during social stress. *American Journal of Gastroenterology*, *114*(7), 1152-1162. doi: 10.14309/ajg.0000000000000203

Multi-omics Data Analysis Reveals Metabolic Adaptations in Cats with Chronic Kidney Disease

Qinghong (Johnny) Li, PhD
Nestlé Purina, MO, USA
qinghong.li@rd.nestle.com

This presentation included unpublished data that is pending review for publication. Therefore, an abstract has been provided below.

Abstract

Chronic kidney disease (CKD) is the leading cause of mortality in aged cats. After injury, feline kidneys undergo extensive metabolic reprogramming, but a comprehensive evaluation is lacking. Integration of serum metabolome from 15 early stages, 6 late stages CKD and 14 healthy control cats with renal cortex and medulla transcriptome and proteome reveals spatiotemporal patterns of gene and protein expression changes. In the early stages, there are 6 differentially expressed genes in the cortex, but ~2000 in the medulla. The number in the cortex increases to >4000 in late stages. The study provides evidence of deranged bioenergetics in CKD: circulating fatty acids and acylcarnitines accumulate, while genes and proteins involved in fatty acid transport and oxidation are downregulated. Glucose and pyruvate metabolism is altered. Impaired glutamine metabolism contributes to both energy deficiency and acid-base imbalance. Additionally, there is a downregulation of redox enzymes, and overexpression of proinflammatory mediators in CKD. Gene expression of TGFβ1 is strongly and positively correlated with that of other fibrogenic genes. Finally, hypoxia signaling pathway is upregulated, and negatively correlated with SGLT2 expression. These data unveil profound metabolic abnormalities in feline CKD.

Machine Learning and In Silico Modeling

Ebenezer Satyaraj, PhD
Nestle Research Saint Louis, MO, USA
ebenezer.satyaraj@rd.nestle.com

Chang Woon Jang, PhD
Nestle Research Saint Louis, MO, USA
changwoon.jang@rd.nestle.com

Glossary of Abbreviations

HF	heart failure
ML	machine learning
MMVD	myxomatous mitral valve disease
SVM	support vector machine

Introduction

In-silico modeling is a powerful tool used in biological research, offering significant advantages over traditional laboratory methods by allowing virtual experimentation that saves time and resources.[1] This approach enables the simulation of complex biological phenomena, providing valuable insights into the dynamics, design, and evolution of biological systems. Additionally, in-silico modeling aids in predicting the behavior of these systems under various conditions, facilitating hypothesis generation and testing.[2] Overall, it is a versatile and impactful method that advances our understanding of biological systems and supports the development of novel nutritional solutions.[3]

Machine learning (ML) approach handles vast amounts of complex biological data, such as genomic sequences, protein structures, and metabolic pathways.[4] ML algorithms can process and analyze these large datasets efficiently, uncovering patterns and insights that might be missed by traditional methods.[5] In addition, ML can create the predictive models to forecast biological outcomes. For example, it can predict disease progression, small molecule responses, or the effects of genetic mutations. These models help in understanding and potentially mitigating health issues. Overall, the ability of ML to handle and analyze complex biological data makes it an invaluable tool in advancing our understanding of biology and improving healthcare outcomes.

In this presentation, we will explore the application of in-silico modeling and machine learning approaches to advance our research in companion animal nutrition. By leveraging computational simulation and predictive algorithms, we aim to optimize nutritional formulations, enhance ingredient selection, and improve overall pet health benefits. Our innovative methods allow us to analyze vast datasets, uncover hidden patterns, and make data-driven decisions that contribute to the development of novel nutritional solutions.

Protein-Ligand Molecular Docking Simulation

Molecular docking simulations can play a pivotal role in the development of innovative, safe, and high-quality nutritional solutions, profoundly influencing the field of food science& nutrition.[6,7] These simulations enable the prediction of interactions between molecular receptors and bioactive peptides derived from diet at the molecular level, which is essential for the creation of functional foods with specific health benefits. The utilization of docking simulations significantly reduces the need for extensive laboratory experiments, thereby saving time and resources and enhancing the efficiency and cost-effectiveness of the research process. This approach allows for the rapid identification of effective compounds from a vast amount of natural compounds present in dietary ingredients. In our study, we employed in-silico screening and docking simulations to identify compounds with high affinity for the target receptor. The docking simulation process encompasses several critical steps, including:

1. **Molecule Preparation:** Both the compounds and target proteins are optimized and prepared in the correct form for docking.
2. **Binding Site Selection:** The binding site on the target protein, typically a pocket where the ligand is likely to bind, is identified.
3. **Docking Process:** The compound is virtually docked into the binding site of the target protein using various algorithms to explore different orientations and conformations of the ligand within the binding site.
4. **Scoring Function:** Each potential binding orientation is evaluated using scoring functions to estimate the strength and stability of the interaction between the ligand and the target protein.
5. **Analysis:** The best-scoring orientations are analyzed to understand the binding interactions, including hydrogen bonds, hydrophobic interactions, and electrostatic forces.

The binding affinity of a ligand is calculated using a scoring function that integrates multiple components to estimate the free energy of binding. Autodock Vina[8,9] uses an empirical scoring function, derived from experimental data and statistical analysis, to estimate binding affinity by summing various energy terms. These terms include steric interactions, hydrogen bonding, desolvation, and rotational and translational entropy. Steric interactions are modeled using a Lennard-Jones potential to represent van der Waals forces as follows:

$$V(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] \tag{1}$$

where $V(r)$ is potential energy as a function of energy of distance r between two atoms, ε is the strength of the interaction, σ is the finite distance at which the inter-particle potential is zero and r is the distance between two atoms. Hydrogen bonding interactions are modeled using a term that incorporates both the geometric and energetic characteristics of hydrogen bonds. This function is generally expressed as follows:

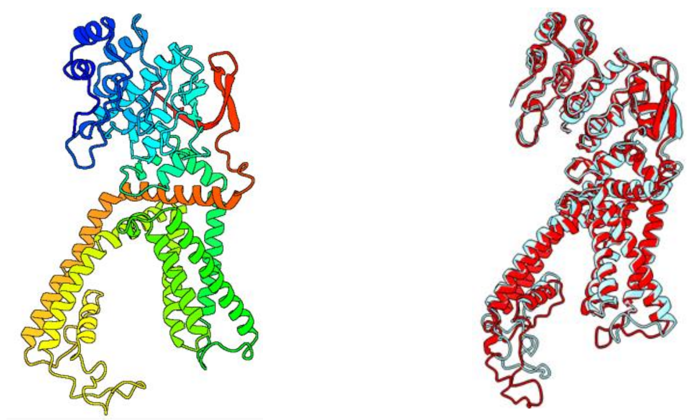
$$E_{HB} = \frac{C_{HB}}{r_{HB}^2} \tag{2}$$

where E_{HB} is the energy contribution from hydrogen bonding, C_{HB} is a constant that represents the strength of the hydrogen bond, and r_{HB} is the distance between the hydrogen donor and acceptor atoms. The desolvation term estimates the energy change that occurs when water molecules are removed from the binding site as the ligand binds to the target. This term's functional form is expressed as follows:

$$E_{desolvation} = \sum_{i,j} S_{ij} \cdot \Delta G_{solvation}(i,j) \tag{3}$$

where $E_{desolvation}$ is the desolvation energy, S_{ij} is a solvation parameter that depends on the types of atoms i and j, and $\Delta G_{solvation}(i,j)$ is the solvation free energy change for atoms i and j. The specific functional form of the rotational and translational entropy terms is not explicitly described. Nevertheless, the scoring function incorporates an empirical penalty to account for the loss of these entropies upon binding. This penalty is quantified as a constant value multiplied by the number of rotatable bonds in the ligand.

Figure 1(a) presents the predicted canine receptor model employed in this study. ***Figure 1(b)*** depicts a comparative analysis between the human crystal receptor structure (cyan) and the predicted canine receptor model (red), derived from protein sequences. The superimposition of these structures reveals a high degree of conformational similarity. Based on this structural resemblance, as demonstrated in ***Figure 2(b)***, we propose that the binding pocket of the canine receptor is likely positioned analogously to that of the human receptor.



(a) (b)

Figure 1. (a) The receptor model targeted in this study. ***(b)*** Comparative analysis with the human receptor crystal structure. The overall conformation of the two structures exhibits significant similarity.

Docking validation with the existing crystal structure complex is necessary before screening other compounds because it ensures the accuracy and reliability of the docking results, helping to identify the promising compounds for further product development. The simulation accurately predicted the ligand binding pose on the model structure, as illustrated in ***Figure 2***. The reference compound (cyan) binds to the active binding pocket, and its predicted binding pose (red) closely matches the crystal structure.

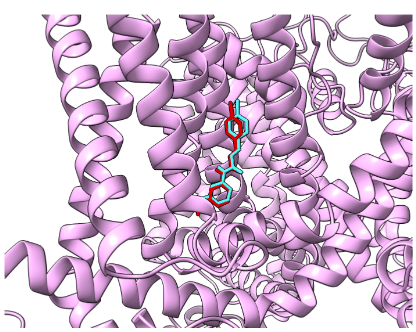


Figure 2. Docking validation was confirmed using the reference (cyan) crystal structure. The predicted binding pose was well-positioned to mimic the ligand crystal structure (cyan).

After identifying the binding pocket and validating the docking process, a large number of compounds were positioned in the specified binding site, and their binding energies were calculated to assess affinity strength. As shown in ***Figure 3***, compound 1 (pink) was docked in the binding site with a binding energy of -10.5 kcal/mol, whereas the reference compound (light blue) exhibited a binding energy of -8.2 kcal/mol. All compounds were ranked based on their binding energies to prioritize them for further study or development. In principle, lower binding energies (in kcal/mol) indicate better affinity.

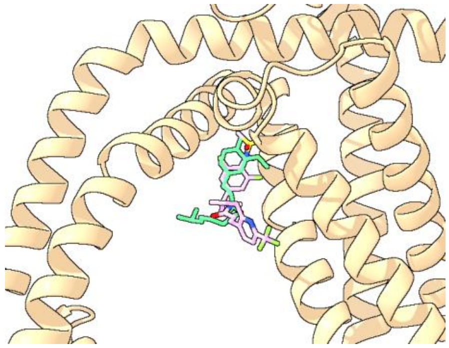


Figure 3. Compound 1 (pink) and the reference compound (light blue) are shown binding to the receptor with binding energies of -10.5 kcal/mol and -8.2 kcal/mol, respectively.

Several thousand compounds were screened. In Autodock Vina, a binding affinity threshold value of -7.0 kcal/mol is typically considered good. Values below this threshold generally indicate strong binding between the ligand and the receptor. However, the exact threshold can vary depending on the specific system and context of the study. The binding energy, also referred to as binding affinity, of various natural compounds was predicted as illustrated in ***Figure 4***. A lower binding energy indicates a higher binding affinity to the receptor.

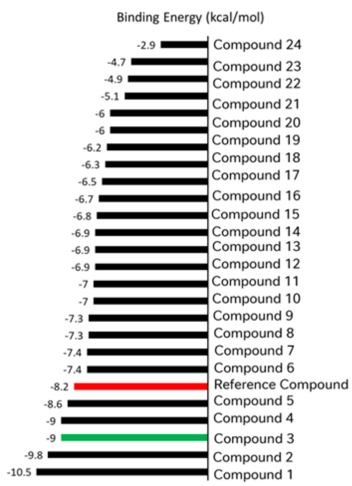
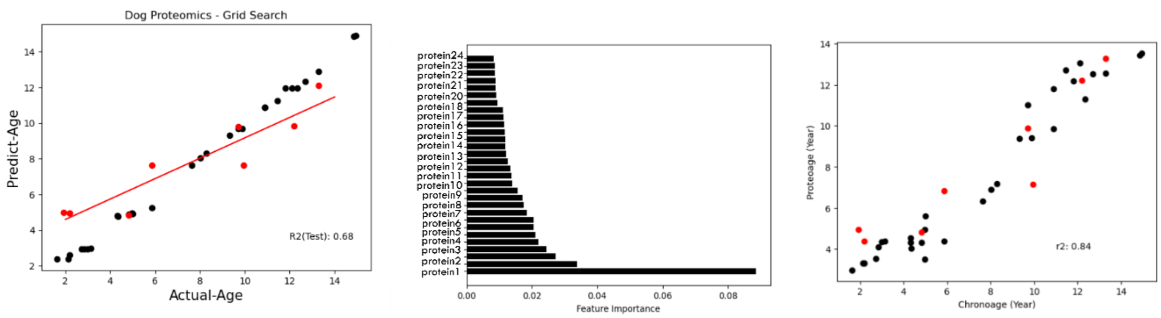


Figure 4. Binding energies were estimated through protein-ligand docking simulations. Five compounds exhibited superior binding affinity compared to the reference compound.

Data-driven Machine Learning Study

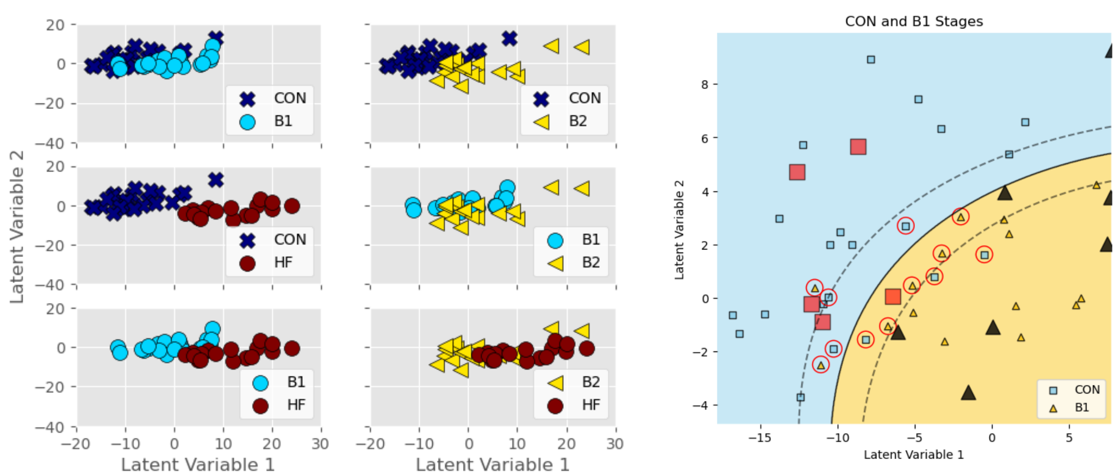
Machine learning (ML) models were developed to predict canine biological age using proteomic data and to assess the progression of myxomatous mitral valve disease (MMVD) using metabolomic data from urine or blood samples, employing various algorithms to analyze and classify the relevant biological markers. These models provide valuable insights for understanding aging in dogs and managing the progression of MMVD.[10] The initial biological-age model exhibited suboptimal performance, with an R-squared value of 0.68 when utilizing the entire dataset of 3000 proteins, as depicted in ***Figure 5(a)***. However, after identifying 24 key protein biomarkers from the 3000 proteins and re-training the model using only these key proteins, its performance improved significantly, achieving an R-squared value of 0.84, as shown in ***Figure 5(c)***.



(a) (b) (c)

Figure 5. Machine learning model predicts ***(a)*** canine biological age and identifies ***(b)*** 24 key biomarkers from 3000 protein profile. These biomarkers enhance ***(c)*** the prediction performance of the model.

The progression of canine myxomatous mitral valve disease (MMVD) was analyzed within the latent space, as depicted in ***Figure 6(a)***. The disease progression is categorized into four distinct stages: healthy control (CON), initial stage of MMVD (B1), intermediate stage of MMVD (B2), and heart failure (HF). Notably, the health control group (dark blue) is distinctly separated from the heart failure group (brown), as illustrated in ***Figure 6(a)***. The early progression of MMVD (B1) was also distinguished from the healthy control group (CON) with an accuracy of 85%, as shown in ***Figure 6(b)***.



(a) (b)

Figure 6. (a) The machine learning model predicts the progression of canine myxomatous mitral valve disease (MMVD). As the disease advances, each group becomes distinct, with symbols moving to the right in the latent space. The health control (CON) and heart failure (HF) groups are completely classified. ***(b)*** The support vector machine (SVM) distinguishes between healthy control (CON) and the first stage (B1) of MMVD with an accuracy of 85%.

Conclusion

In-silico modeling and machine learning techniques offer numerous advantages in research and development of novel nutritional solutions. Protein-ligand docking simulations enable the rapid and efficient screening of large compound libraries to identify those most likely to bind to target proteins, while also optimizing lead compounds for enhanced effectiveness. This approach is both cost-effective and faster than traditional experimental methods, making molecular docking an essential tool for preliminary studies prior to more expensive research studies.

Additionally, we have developed machine learning algorithms have been applied to estimate the biological age of dogs using proteomic data and to predict the progression of canine myxomatous mitral valve disease (MMVD) through metabolomic data. The careful selection of specific protein biomarkers significantly enhanced the performance of these models compared to those utilizing the entire protein profile. Notably, the classification model for predicting stages of MMVD achieved over 85% accuracy in distinguishing between healthy dogs and those in the early stages of the disease.

Overall, these computational techniques provide substantial benefits in nutritional discovery. Molecular docking simulations facilitate rapid compound screening and lead optimization, while machine learning algorithms enhance the prediction and classification of canine diseases, demonstrating high accuracy in identifying disease stages and estimating biological age. Together, these technologies streamline research, making them invaluable tools for developing novel nutritional solutions.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Barh, D., Chaitankar, V., Yiannakopoulou, E. C., Salawu, E. O., Chowbina, S., Ghosh, P., & Azevedo, V. (2013). In silico models: From simple networks to complex diseases. *Animal Biotechnology: Models in Discovery and Translation*, *15*, 385–404. doi: 10.1016/B978-0-12-416002-6.00021-3
2. Mercado, J. C., & Picardal, J. P. (2023). Virtual Laboratory Simulations in Biotechnology: A Systematic Review. *Science Education International*, *34*(1), 52-57. doi: 10.33828/sei.v34.i1.6
3. Vashishat, A., Patel, P., Gupta, G. D., & Kurmi, B. D., (2024). Alternatives of animal models for biomedical research: A comprehensive review of modern approaches. *Stem Cell Reviews and Reports*, *20*, 881-899. doi: 10.1007/s12015-024-10701-x
4. Xu, C., & Jackson, S. A. (2019). Machine learning and complex biological data. *Genome Biology*, *20*, 76. doi: 10.1186/s13059-019-1689-0
5. Milite, S., Caravagna, G., & Sottoriva, A. (2025). MIDAA: deep archetypal analysis for interpretable multi-omic data integration based on biological principles. *Genome Biology*, *26*, 90. doi: 10.1186/s13059-025-03530-9
6. Tao, X., Huang, Y., Wang, C., Chen, F., Yang, L., Ling, L., Che, Z., & Chen, X. (2020). Recent developments in molecular docking technology applied in food science: a review. *International Journal of Food Science and Technology*, *55*(1), 33-45. doi: 10.1111/ijfs.14325
7. Khan, T., Lawrence, A. J., Azad, I., Raza, S., & Khan, A. R. (2018). Molecular docking simulation with special reference to flexible docking approach. *JSM Chemistry*, *6*(1), 1053. doi: 10.47739/2334-1831/1053
8. Eberhardt, J., Santos-Martins, D., Tillack, A.F., & Forli, S. (2021). AutoDock Vina 1.2.0: New docking methods, expanded force field, and Python bindings. *Journal of Chemical Information and Modeling*, *61*(8), 3891-3898. doi: 10.1021/acs.jcim.1c00203
9. Trott, O., & Olson, A. J. (2010). AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *Journal of Computational Chemistry*, *31*(2), 455-461. doi: 10.1002/jcc.21334
10. Li, Q., Larouche-Lebel, É., Loughran, K. A., Huh, T. P., Suchodolski, J. S., & Oyama, M. A. (2021). Metabolomics analysis reveals deranged energy metabolism and amino acid metabolic reprogramming in dogs with myxomatous mitral valve disease. *Journal of the American Heart Association*, *10*(9), e018923. doi:10.1161/JAHA.120.018923

Holistic Integration of Omics Tools for Precision Nutrition

Omar Ramos-Lopez, PhD
Medicine and Psychology School, Autonomous University of Baja California, Tijuana, Baja California, Mexico
oscar.omar.ramos.lopez@uabc.edu.mx

Glossary of Abbreviations

NCDs Non-communicable diseases
T2D Type 2 diabetes
CVD Cardiovascular disease
PN Precision nutrition
SNPs Single nucleotide polymorphisms
ML Machine learning

Introduction

In general, malnutrition (undernutrition and overnutrition) is considered one of the main factors contributing to the global burden of non-communicable diseases (NCDs) such as obesity, metabolic syndrome, type 2 diabetes (T2D), hypertension, cardiovascular disease (CVD), liver damage, and some types of cancer. The chronic consumption of high-calorie diets rich in sugar, saturated fat, and sodium, as well as deficiencies in specific essential nutrients, contribute substantially to the rising prevalence of these diseases.[1] In response to this important challenge, national and international guidelines and general recommendations have been established to promote healthy nutritional habits and lifestyles, although these have had a minimal impact. This may be partly related to the fact that the "single or total diet" nature of these dietary guidelines does not consider the biological and sociocultural factors driving human eating behavior, which has led to the development of tailored strategies to improve dietary patterns and public health. In this context, Precision Nutrition (PN) is defined as a methodology to integrate multiple information at scale to developing targeted and comprehensive nutritional recommendations for individuals and population subgroups.[2] In fact, PN includes genetic, epigenetic, metagenomic and metabolomics insights from high-throughput technologies for the global analysis and characterization of large sets of biological molecules involving diverse metabolic pathways, with a wide spectrum of bioinformatics data and analytical tools. PN also takes into account socioeconomic and psychosocial characteristics, food environments, and other clinical features such as perinatal feeding, health status, circadian rhythm, dietary patterns, eating behaviors, and physical activity. Moreover, the integration of nutrition with omics technologies has given rise to "nutriomics", whose term refers to the emerging areas of nutrigenomics, nutrigenetics, nutriepigenetics, nutrimetabolomics, and nutrimetagenomics to the better understanding of the complex interactions between nutrients, diet, and the human body's molecular processes.[3] This document provides an overview of nutriomics to guide their application in clinical and public health as well as visualize the integration of these disciplines into a holistic approach for PN in health and disease.

Nutrigenetics

Nutrigenetics focuses on studying responses to foods or diets based on each person's genotype. Genome-wide sequencing studies and candidate-gene approaches have identified a number of mutations, structural variants or genetic polymorphisms influencing individual health outcomes upon dietary consumption, which are mapped to genes regulating adipogenesis, energy intake, appetite, taste perception, lipid metabolism, insulin resistance, and inflammation.[4] Indeed, single nucleotide polymorphisms (SNPs) are the most widely studied genetic variations in the field of PN. In a first approach, nutrigenetic studies have identified SNPs associated with NCDs by interacting with dietary factors. Examples include SNPs in genes involved in one-carbon metabolism, such as *MTR* and *MTHFR*, which may increase the risk for breast cancer in genetically susceptible individuals with dietary deficiencies of folate, vitamin B6, and vitamin B12.[5] Also, an increased risk of hypertension[6] and CVD[7] was reported in moderate and heavy coffee drinkers carrying the *CYP1A2* rs762551 SNP. Likewise, SNPs in the *VDR* gene were associated with the presence of osteoporosis in postmenopausal women with low calcium intakes.[8] Whereas, SNPs in lipid-related genes such as *APOA1* and *APOC3* were linked to metabolic syndrome predisposition in subjects adopting a Westernized dietary pattern.[9] In a second approach, studies have analyzed relevant SNPs-diet interactions related to the heterogeneous responses to nutritional interventions aimed at weight loss or metabolic improvements. For instance, overweight individuals carrying the risk allele of the *FTO* rs1558902 SNP underwent greater reductions in body weight, body composition, and fat distribution after consuming a high-protein diet, whereas an opposite genetic effect was observed in response to a low-protein diet.[10] Similarly, greater decreases in blood cholesterol and LDL-c were found in carries of the *APOA5* rs964184 SNP upon the intake of a low-fat diet.[11] Besides, a high-carbohydrate diet led to better improvements of insulin resistance measurements in participants with the *IRS1* rs2943641 SNP than those without this variant. Furthermore, a third approach consist of evaluate disclosure of nutrigenetic tests on modifying eating habits. In this regard, participants receiving information concerning a risk version of the *ACE* gene significantly reduced their sodium intake after be advised about the risks of high-sodium consumption and implications of genetic susceptibility, as compared to the control group.[12] Also, individuals who were informed about their *FADS1* genotype reported fewer barriers for the consumption of omega-3 fatty acids and were more aware of their beneficial role on health, as compared with those who did not receive their personal genetic information.[13] In addition, participants who received personalized nutrition targeting SNPs in nutrient-responsive genes showed greater Mediterranean diet scores than those who received conventional dietary advice.[14]

Nutrigenomics

Nutrigenomics refers to the study of the role of diet or nutrients on gene expression regulating critical metabolic pathways, whose alterations are linked to the onset of metabolic disturbances and diseases. For instance, it has been reported that consumption of a Western dietary pattern (characterized by high intakes of red and processed meats, sugary drinks, dairy and refined grain products, and industrialized foods) may increase the expression of genes related to inflammatory response and cancer signaling than those consuming high amounts of fruits, vegetables, and whole grains.[15] High-fat/high sugar diets have also shown to induce upregulation of genes involved in glucose intolerance, insulin resistance, inflammation, hepatic lipid accumulation, and obesity development.[4] Meanwhile, diets with deficiencies in micronutrients such as choline, folate, chromium, selenium, vitamin B12, and vitamin A could increase the risk of fatty liver, T2DM, and CVD via dysregulation of lipogenic, insulin signaling, and proinflammatory genes.[4] On the other hand, the beneficial health effects of some diets have been related to particular gene expression profiles. In this sense, adherence to the Mediterranean diet significantly reduced the postprandial expression of proinflammatory and proatherogenic genes.[16] Also, high intakes of monounsaturated and polyunsaturated fatty acids favorably regulated the expression of genes related to energy homeostasis, fatty acid oxidation, lipid storage, and immune response.[17,18]

Moreover, it has been reported that bioactive food compounds such as sulforaphane, epigallocatechin-3-gallate, theaflavin, and genistein exert anticancer effects by upregulating tumor suppressor genes, whereas curcumin and resveratrol have shown antiatherogenic properties by downregulating genes involved in plaque formation.[4] Of note, differentially expressed genes have been identified concerning the success of weight loss after energy-restriction programs, where individuals who regained body weight after the intervention overexpressed genes related to cell death and inflammation, whereas subjects with continued weight loss showed upregulation of genes participating in mitochondrial oxidative phosphorylation.[19] Additionally, the positive effects of weight loss were related to reduced expression of the oncogene survivin upon very low-calorie diet or bariatric surgery, whose expression levels were comparable to those with normal weight.[20]

Nutriepigenetics

Epigenetics investigates heritable changes in gene expression that are not attributable to adjacent alterations in the DNA coding sequence. DNA methylation status, non-covalent histone modifications, and miRNA expressions are the most studied epigenetic signatures that are modifiable and susceptible to environmental factors such as diet. Thus, nutriepigenetic research focuses on the study of the effects of foods and nutrients on the epigenome that may impact the cellular phenotype.[21] Complex interactions between diet and epigenetic marks have been implicated in disease susceptibility. For example, low folate intake has been associated with obesity features and insulin resistance involving hypomethylation of the *CAMKK2* gene.[22] Also, deficiencies of nutrients such as magnesium, chromium, and vitamin D could increase the risk of suffering T2D by promoting methylation aberrations in genes regulating glucose homeostasis and insulin signaling.[4] Besides, high-fat diets have been associated with obesity susceptibility via abnormal methylation of neuropeptide genes controlling food intake.[23] Some experimental studies have investigated the epigenomic effects of healthy foods and diets. Thus, high fruit consumption was related to better glucose tolerance partially mediated by lower methylation of the inflammatory *TNFA* gene in young adults.[24] Likewise, high adherence to the Mediterranean diet was associated with hypermethylation of inflammatory genes in subjects at high cardiovascular risk.[25] Hypomethylation and acetylation of tumor suppressor genes and increases of miRNAs targeting oncogenes were some of the epigenetic modifications underlying the anticancer properties of bioactive food compounds including genistein, sulforaphane, resveratrol, epigallocatechin-3-gallate, and curcumin.[4] Moreover, apple polyphenols prevented diet-induced obesity by modulating the methylation status of lipid metabolism genes.[26] Furthermore, some epigenetic marks have mirrored health outcomes after dietary counseling. Interestingly, changes in the DNA methylation status of the circadian gene *BMAL1* accompanying the lipid-lowering effects of a hypocaloric diet intervention in women.[27] Besides, glycemic outcomes in response to weight-loss dietary interventions were linked to regional DNA methylation signatures at the *TXNIP* gene, a key regulator of glucose homeostasis.[28] Additionally, several circulating miRNAs (miR-221-3p, miR-29c-3p, miR-144-5p, miR-15a-5p, miR-130a-3p, miR-142-5p, and miR-22-3p) were able to predict the adiposity responses to a low-fat dietary intervention in overweight individuals.[29]

Nutrimetagenomics

Nutrimetagenomics analyzes the impact of nutrition on the gut microbiome including enterocyte structure, immunity, and energy homeostasis influencing host physiology. Indeed, nutrimetagenomic analyses have allowed the exhaustive study of microbial and host genetic material to find associations between intestinal microbial profiles and dietary patterns or the intake of different foods or nutrients as well as elucidate potential relationships between bacterial species and NCDs.[3] In this context, macronutrients, fibers, fatty acids, polyphenols, and prebiotics have been identified as some of the most influential dietary determinants of the intestinal microbiome.[30] For instance, complex carbohydrates improve energy metabolism and ameliorate inflammatory bowel disease through specific gut microbiota modifications. Also, the antioxidant, anti-inflammatory, cardioprotective, and anticancer properties of polyphenols are related to intestinal bacteria modulation. Besides, whereas plant-derived proteins have shown to maintain gut barrier integrity and improve insulin signaling, animal proteins may promote insulin resistance and atherosclerosis development via microbiota alterations.[30] Subsequent longitudinal analyses revealed increases in the diversity of microbial gene families and beneficial symbiotic functions after consuming a healthy dietary pattern in Chinese population.[31] In addition, some trials have applied nutrimetagenomic approaches to explain individualized responses to dietary intakes. Thus, a diet rich in whole grains induced reductions in obesity-related bacteria after 8 weeks in Danish adults at risk of metabolic syndrome, which could help explain the observed reduction in body weight and low-grade inflammation in these patients.[32] Similarly, 8-week consumption of Brazilian nuts within an energy-restricted program mitigated the altered intestinal permeability and increased beneficial bacteria linked to pathways associated with body fat reduction in overweight women.[33] Therefore, the gut microbiota composition can help to design and implement tailored PN strategies to achieve greater impacts on health and metabolic status at the individual level. Moreover, identifying microbial biomarkers associated with specific diseases may provide valuable targets for therapeutic purposes.

Nutrimetabolomics

Metabolomics is a growing technology that aims to identify and quantify metabolites present in different biological samples (urine, blood, and feces). Its use in nutritional research (nutrimetabolomics) is generating valuable information on the effects of diet on metabolic regulation. Applications of analytical and bioinformatics technologies have led to the rapid adoption of nutrimetabolomic investigations to individualize several pathophysiological conditions and chronic diseases. In particular, the application of nutrimetabolomic approaches has improved the accuracy of dietary assessment by detecting biomarkers of food intake and identifying metabolites that can serve as targets for PN interventions. Thus, metabolomics is currently being used to evaluate the bioavailability of food components and to assess metabolic changes associated with food consumption or adherence to a dietary program. Therefore, metabolomic analyses are making it possible to metabolically categorize individuals into different groups based on their dietary intake or appropriate dietary prescription.[3] Currently, two major metabolomics strategies have been developed: untargeted metabolomics, encompassing an in-depth analysis of all measurable metabolites in a sample; and targeted metabolomics, which is founded on the measurement of well-defined metabolites. Untargeted metabolomics is especially useful when there is no prior metabolic hypothesis, whereas targeted metabolomics yield high sensitivity and selectivity of targets of interest. Certainly, nutrimetabolomic studies have focused on understanding individualized responses to dietary intake and metabolic outcomes. Accordingly, relationships between cocoa consumption and intake biomarkers in plasma have been identified, which in turn were associated with reductions in depressive symptoms.[34] Likewise, a nutrimetabolomic assay supported that the beneficial effects of α-lipoic acid administration on body weight reduction were mediated by its antioxidant properties as well as by the production of related secondary metabolites in urine of overweight/obese women.[35] Also, a nutrimetabolomic analysis identified changes in the serum metabolomic profiles of overweight and obese older adults following a weight loss intervention based on a hypocaloric diet, where concentrations of saturated fatty acids decreased after the intervention and baseline palmitoleic acid was found to be a negative predictor of changes in body fat losses.[36]

Integrating Nutriomics for Precision Nutrition

The integration of multiple nutriomics has emerged as an innovative scope to provide a more holistic view of human metabolism and overall health status of an individual as well as elucidating the molecular and physiological levels underlying NCDs. For this purpose, extracting valuable insights from nutriomics data often needs efficient methods to reach objective conclusions and results. Thus, machine learning (ML) techniques are contributing to integrating and interpreting nutriomic knowledge for early disease prediction, decision-making algorithms, and tailored therapeutic schemes for the precise management of NCDs. For example, an integrated approach with ML was developed to predict obesity using nutriomic data (genetic polymorphisms and DNA methylation sites) and dietary information (specific nutrients and food components), thus extending current knowledge of the drivers of obesity.[37] Also, a ML model was able to predict triglyceride and glycemic responses to food intake by combining genetic, clinical, metabolic, microbiome configuration, and meal context data in twins and unrelated adults.[38] Moreover, an integrative nutri-prototype was modeled based on genetic, phenotypic, and environmental information for the personalized prescription of energy-restricted diets with different macronutrient distribution in overweight/obese subjects, helping to individualize dietary advice for the management of excessive adiposity using PN variables. New frontiers in ML and other artificial intelligence approaches will pave the way to deliver PN, where nutriomics insights can be combined and harmonized with other environmental, lifestyle, sociocultural, and behavioral determinants of health to improve population diets. However, the effective implementation of PN in clinical care need to take into account the ethical, legal, and social issues of the use of genetic information and other highly sensitive personal information, the improvement of the skills and knowledge of health professionals, and multidisciplinary collaborations between researchers, stakeholders, and food industry, where patients should be placed at the center. The global application of PN also requires an understanding of population health, sustainability of diets, political issues, and the technological and digital landscapes of each region. Other challenges include the lack of studies across different populations, and the need for harmonized protocols for data collection and analysis.

Conclusion

The progress and contributions of nutrigenetics, nutrigenomics, nutriepigenetics, nutrimetagenomics, and nutrimetabolomics are essential for better understanding of human nutrient metabolism, identification and characterization of molecular targets and active biomarkers involved in many NCDs as well as developing innovative managing strategies through a holistic PN approach. This knowledge will be enhanced by advances in bioinformatics, integrative software, ML, and other artificial intelligence methods that could be useful for disease risk prediction and early diagnosis purposes, stratifying patients based on common features, and guiding disease treatments and prognosis. However, more evidence in these nutriomics areas is still necessary before PN can be implemented in clinical practice and public health settings worldwide.

Conflicts of Interest

No conflicts of interest to declare

References

1. Bruins, M. J., Van Dael, P., & Eggersdorfer, M. (2019). The role of nutrients in reducing the risk for noncommunicable diseases during aging. *Nutrients, 11*(1), 85. doi: 10.3390/nu11010085
2. Livingstone, K. M., Ramos-Lopez, O., Pérusse, L., Kato, H., Ordovas, J. M., & Martínez, J. A. (2022) Precision nutrition: a review of current approaches and future endeavors. *Trends in Food Science & Technology, 128*, 253–64. doi: 10.1016/j.tifs.2022.08.017
3. Ramos-Lopez, O., Assmann, T. S., Astudillo Muñoz, E. Y., Baquerizo-Sedano, L., Barrón-Cabrera, E., Bernal, C. A., Bressan, J., …Martinez, J. A. (2025). Guidance and Position of RINN22 regarding Precision Nutrition and Nutriomics. *Lifestyle Genomics, 18*(1), 1-19. doi: 10.1159/000542789
4. Ramos-Lopez, O., Milagro, F. I., Allayee, H., Chmurzynska, A., Choi, M. S., Curi, R., De Caterina, R., …Martínez, J. A. (2017). Guide for current nutrigenetic, nutrigenomic, and nutriepigenetic approaches for precision nutrition involving the prevention and management of chronic diseases associated with obesity. *Journal of Nutrigenetics and Nutrigenomics, 10*(1-2), 43-62. doi: 10.1159/000477729
5. Jiang-Hua, Q., De-Chuang, J., Zhen-Duo, L., Shu-de, C., & Zhenzhen, L. (2014). Association of methylenetetrahydrofolate reductase and methionine synthase polymorphisms with breast cancer risk and interaction with folate, vitamin B6, and vitamin B 12 intakes. *Tumour Biology, 35*(12), 11895-901. doi: 10.1007/s13277-014-2456-1
6. Palatini, P., Ceolotto, G., Ragazzo, F., Dorigatti, F., Saladini, F., Papparella, I., Mos, L., Zanata, G., & Santonastaso, M. (2009). CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension. *Journal of Hypertension, 27*(8), 1594-601. doi: 10.1097/HJH.0b013e32832ba850
7. Cornelis, M. C., El-Sohemy, A., Kabagambe, E. K., & Campos, H. (2006). Coffee, CYP1A2 genotype, and risk of myocardial infarction. *Journal of the American Medical Association, 295*(10), 1135-41. doi: 10.1001/jama.295.10.1135
8. Stathopoulou, M. G., Dedoussis, G. V., Trovas, G., Theodoraki, E. V., Katsalira, A., Dontas, I. A., Hammond, N., Deloukas, P., & Lyritis, G. P. (2011). The role of vitamin D receptor gene polymorphisms in the bone mineral density of Greek postmenopausal women with low calcium intake. *Journal of Nutritional Biochemistry, 22*(8), 752-7. doi: 10.1016/j.jnutbio.2010.06.007
9. Hosseini-Esfahani, F., Mirmiran, P., Daneshpour, M. S., Mehrabi, Y., Hedayati, M., Soheilian-Khorzoghi, M., & Azizi, F. (2015). Dietary patterns interact with APOA1/APOC3 polymorphisms to alter the risk of the metabolic syndrome: the Tehran Lipid and Glucose Study. *British Journal of Nutrition, 113*(4), 644-53. doi: 10.1017/S0007114514003687
10. Zhang, X., Qi, Q., Zhang, C., Smith, S. R., Hu, F. B., Sacks, F. M., Bray, G. A., & Qi, L. (2012). FTO genotype and 2-year change in body composition and fat distribution in response to weight-loss diets: the POUNDS LOST Trial. *Diabetes, 61*(11), 3005-11. doi: 10.2337/db11-1799
11. Zhang, X., Qi, Q., Bray, G. A., Hu, F. B., Sacks, F. M., & Qi, L. (2012). APOA5 genotype modulates 2-y changes in lipid profile in response to weight-loss diet intervention: the Pounds Lost Trial. *American Journal of Clinical Nutrition, 96*(4), 917-22. doi: 10.3945/ajcn.112.040907
12. Nielsen, D. E., & El-Sohemy, A. (2014). Disclosure of genetic information and change in dietary intake: a randomized controlled trial. *PLoS One, 9*(11), e112665. doi: 10.1371/journal.pone.0112665
13. Roke, K. (2017). Exploration of the perceived and actual benefits of omega-3 fatty acids and the impact of FADS1 and FADS2 genetic information on dietary intake and blood levels of EPA and DHA. *Applied Physiology, Nutrition, and Metabolism, 42*(3), 333. doi: 10.1139/apnm-2016-0700
14. Livingstone, K. M., Celis-Morales, C., Navas-Carretero, S., San-Cristobal, R., Macready, A. L., Fallaize, R., Forster, H., …Food4Me Study. (2016). Effect of an Internet-based, personalized nutrition randomized trial on dietary changes associated with the Mediterranean diet: the Food4Me Study. *American Journal of Clinical Nutrition, 104*(2), 288-97. doi: 10.3945/ajcn.115.129049
15. Bouchard-Mercier, A., Paradis, A. M., Rudkowska, I., Lemieux, S., Couture, P., & Vohl, M. C. (2013). Associations between dietary patterns and gene expression profiles of healthy men and women: a cross-sectional study. *Nutrition Journal, 12*, 24. doi: 10.1186/1475-2891-12-24
16. Camargo, A., Delgado-Lista, J., Garcia-Rios, A., Cruz-Teno, C., Yubero-Serrano, E. M., Perez-Martinez, P., Gutierrez-Mariscal, F. M., …Lopez-Miranda, J. (2012). Expression of proinflammatory, proatherogenic genes is reduced by the Mediterranean diet in elderly people. *British Journal of Nutrition, 108*(3), 500-8. doi: 10.1017/S0007114511005812
17. Varela, L. M., Ortega-Gomez, A., Lopez, S., Abia, R., Muriana, F. J., & Bermudez, B. (2013). The effects of dietary fatty acids on the postprandial triglyceride-rich lipoprotein/apoB48 receptor axis in human monocyte/macrophage cells. *Journal of Nutritional Biochemistry, 24*(12), 2031-9. doi: 10.1016/j.jnutbio.2013.07.004

18. Dziedzic, B., Szemraj, J., Bartkowiak, J., & Walczewska, A. (2007). Various dietary fats differentially change the gene expression of neuropeptides involved in body weight regulation in rats. *Journal of Neuroendocrinology, 19*(5), 364-73. doi: 10.1111/j.1365-2826.2007.01541.x
19. Márquez-Quiñones, A., Mutch, D. M., Debard, C., Wang, P., Combes, M., Roussel, B., Holst, C., ...DiOGenes Project. (2010). Adipose tissue transcriptome reflects variations between subjects with continued weight loss and subjects regaining weight 6 mo after caloric restriction independent of energy intake. *American Journal of Clinical Nutrition, 92*(4), 975-84. doi: 10.3945/ajcn.2010.29808
20. Izquierdo, A. G., Carreira, M. C., Rodriguez-Carnero, G., Fernandez-Quintela, A., Sueiro, A. M., Martinez-Olmos, M. A., Guzman, G., ...Crujeiras, A. B. (2021). Weight loss normalizes enhanced expression of the oncogene survivin in visceral adipose tissue and blood leukocytes from individuals with obesity. *International Journal of Obesity (London), 45*(1), 206-216. doi: 10.1038/s41366-020-0630-7
21. Li, X., & Qi, L. (2022). Epigenetics in precision nutrition. *Journal of Personalized Medicine, 12*(4), 533. doi: 10.3390/jpm12040533
22. Ramos-Lopez, O., Samblas, M., Milagro, F. I., Zulet, M. A., Mansego, M. L., Riezu-Boj, J. I., & Martinez, J. A. (2018). Association of low dietary folate intake with lower CAMKK2 gene methylation, adiposity, and insulin resistance in obese subjects. *Nutrition Research, 50*, 53-62. doi: 10.1016/j.nutres.2017.11.007
23. Vucetic, Z., Kimmel, J., Totoki, K., Hollenbeck, E., & Reyes, T. M. (2010). Maternal high-fat diet alters methylation and gene expression of dopamine and opioid-related genes. *Endocrinology, 151*(10), 4756-64. doi: 10.1210/en.2010-0505
24. Carraro, J. C., Hermsdorff, H. H., Mansego, M. L., Zulet, M. Á., Milagro, F. I., Bressan, J., & Martínez, J. A. (2016). Higher fruit intake is related to TNF-α hypomethylation and better glucose tolerance in healthy subjects. *Journal of Nutrigenetics and Nutrigenomics, 9*(2-4), 95-105. doi: 10.1159/000448101
25. Arpón, A., Riezu-Boj, J. I., Milagro, F. I., Marti, A., Razquin, C., Martínez-González, M. A., Corella, D., ...Martínez, J. A. (2016). Adherence to Mediterranean diet is associated with methylation changes in inflammation-related genes in peripheral blood cells. *Journal of Physiology and Biochemistry, 73*(3), 445-455. doi: 10.1007/s13105-017-0552-6
26. Boqué, N., de la Iglesia, R., de la Garza, A. L., Milagro, F. I., Olivares, M., Bañuelos, O., Soria, A. C., ...Campión, J. (2013). Prevention of diet-induced obesity by apple polyphenols in Wistar rats through regulation of adipocyte gene expression and DNA methylation patterns. *Molecular Nutrition and Food Research, 57*(8), 1473-8. doi: 10.1002/mnfr.201200686
27. Samblas, M., Milagro, F. I., Gómez-Abellán, P., Martínez, J. A., & Garaulet, M. (2016). Methylation on the circadian gene BMAL1 is associated with the effects of a weight loss intervention on serum lipid levels. *Journal of Biological Rhythms, 31*(3), 308-17. doi: 10.1177/0748730416629247
28. Li, X., Shao, X., Bazzano, L. A., Xue, Q., Koseva, B. S., Grundberg, E., Shai, I., Bray, G. A., Sacks, F. M., & Qi, L. (2022). Blood DNA methylation at TXNIP and glycemic changes in response to weight-loss diet interventions: the POUNDS lost trial. *International Journal of Obesity (London), 46*(6), 1122-1127. doi: 10.1038/s41366-022-01084-5
29. Assmann, T. S., Riezu-Boj, J. I., Milagro, F. I., & Martínez, J. A. (2020). Circulating adiposity-related microRNAs as predictors of the response to a low-fat diet in subjects with obesity. *Journal of Cellular and Molecular Medicine, 24*(5), 2956-2967. doi: 10.1111/jcmm.14920
30. Danneskiold-Samsøe, N. B., Dias de Freitas Queiroz Barros, H., Santos, R., Bicas, J. L., Cazarin, C. B. B., Madsen, L., Kristiansen, K., Pastore, G. M., Brix, S., & Maróstica Júnior, M. R. (2019). Interplay between food and gut microbiota in health and disease. *Food Research International, 115*, 23-31. doi: 10.1016/j.foodres.2018.07.043
31. Yu, D., Yang, Y., Long, J., Xu, W., Cai, Q., Wu, J., Cai, H., Zheng, W., & Shu, X. O. (2021). Long-term diet quality and gut microbiome functionality: A prospective, shotgun metagenomic study among urban Chinese adults. *Current Developments in Nutrition, 5*(4), nzab026. doi: 10.1093/cdn/nzab026
32. Roager, H. M., Vogt, J. K., Kristensen, M., Hansen, L. B. S., Ibrügger, S., Mærkedahl, R. B., Bahl, M. I., ...Licht, T. R. (2019). Whole grain-rich diet reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial. *Gut, 68*(1), 83-93. doi: 10.1136/gutjnl-2017-314786
33. Kelly Souza Silveira, B., Mayumi Usuda Prado Rocha, D., Stampini Duarte Martino, H., Grancieri, M., Juste Contin Gomes, M., Cuquetto Mantovani, H., Bressan, J., & Hermana Miranda Hermsdorff, H. (2024). Daily cashew and Brazil nut consumption modifies intestinal health in overweight women on energy-restricted intervention: A randomized controlled trial (Brazilian Nuts Study). *Journal of Nutrition, 154*(3), 962-977. doi: 10.1016/j.tjnut.2023.12.022
34. Ibero-Baraibar, I., Perez-Cornago, A., Ramirez, M. J., Martínez, J. A., & Zulet, M. A. (2015). An increase in plasma homovanillic acid with cocoa extract consumption is associated with the alleviation of depressive symptoms in

overweight or obese adults on an energy restricted diet in a randomized controlled trial. *Journal of Nutrition, 146*(4), 897S-904S. doi: 10.3945/jn.115.222828

35. Romo-Hualde, A., Huerta, A. E., González-Navarro, C. J., Ramos-López, O., Moreno-Aliaga, M. J., & Martínez, J' A. (2018). Untargeted metabolomic on urine samples after α-lipoic acid and/or eicosapentaenoic acid supplementation in healthy overweight/obese women. *Lipids in Health and Disease, 17*(1), 103. doi: 10.1186/s12944-018-0750-4
36. Perez-Cornago, A., Brennan, L., Ibero-Baraibar, I., Hermsdorff, H. H., O'Gorman, A., Zulet, M. A., & Martínez, J. A. (2014). Metabolomics identifies changes in fatty acid and amino acid profiles in serum of overweight older adults following a weight loss intervention. *Journal of Physiology and Biochemistry, 70*(2), 593-602. doi: 10.1007/s13105-013-0311-2
37. Lee, Y. C., Christensen, J. J., Parnell, L. D., Smith, C. E., Shao, J., McKeown. N. M., Ordovás, J. M., & Lai, C. Q. (2022). Using machine learning to predict obesity based on genome-wide and epigenome-wide gene-gne and gene-diet interactions. *Frontiers in Genetics, 12*, 783845. doi: 10.3389/fgene.2021.783845
38. Berry, S. E., Valdes, A. M., Drew, D. A., Asnicar, F., Mazidi, M., Wolf, J., Capdevila, J., ...Spector, T. D. (2020). Human postprandial responses to food and potential for precision nutrition. *Nature Medicine, 26*(6):964-973. doi: 10.1038/s41591-020-0934-0. Erratum in: *Nature Medicine, 26*(11), 1802. doi: 10.1038/s41591-020-1130-y

The Role of Biomarkers in Veterinary Nutrition and Clinical Practice

Amanda Nascimento, DVM, MS, PhD, ABVT Candidate
IDEXX Laboratories, ME, US
Amanda-nascimento@idexx.com

Glossary of Abbreviations

BUN	blood urea nitrogen
CKD	chronic kidney disease
CRP	C-reactive protein
ctDNA	circulating tumor DNA
IgE	immunoglobulin E
IRIS	International Renal Interest Society
SDMA	symmetric dimethylarginine
TK1	thymidine kinase 1

Introduction

Biomarkers are biological indicators that signal normal or pathogenic processes and may serve as tools for early disease detection, monitoring, and guiding treatment decisions. In veterinary medicine, these indicators are essential for assessing overall health, tailoring dietary interventions, and managing chronic conditions. The application of biomarkers spans multiple clinical areas, including metabolic disorders, renal disease, allergies, gastrointestinal health, endocrine dysfunctions, and even cancer diagnostics. Moreover, in veterinary nutrition, biomarkers play a key role in guiding precision nutrition strategies that optimize pet health outcomes by allowing practitioners to modify diets based on individual metabolic and disease profiles.[1,2]

Biomarkers in Obesity and Metabolic Disorders

Obesity in companion animals is a growing concern. Recent studies indicate that approximately 59% of dogs and 61% of cats in the U.S. are overweight or obese.[3] Several biomarkers can provide insight into metabolic dysfunction, for example:

- **Leptin:** Secreted by adipose tissue, leptin is crucial in regulating appetite and energy balance. Elevated leptin levels in obesity can suggest there is presence of leptin resistance.[2]
- **Adiponectin:** This anti-inflammatory adipokine is typically lower in obese animals and is associated with insulin resistance.
- **Insulin and Glucose:** Elevated levels of these markers may indicate an increased risk for diabetes or insulin resistance.[4]

Clinical Applications and Dietary Interventions:

Monitoring these biomarkers may facilitate early detection of metabolic issues, guide the implementation of high-protein, high-fiber diets, and support the inclusion of omega-3 supplementation for example to that may help improve metabolic function and overall health.[4,5]

Kidney Disease (CKD) - Renal Biomarkers

Early detection of renal dysfunction may be critical for slowing the progression of chronic kidney disease (CKD). Some key renal biomarkers include:

- **SDMA:** Recognized as a reliable early indicator for kidney dysfunction, SDMA levels rise before creatinine in CKD.[6]
- **Creatinine:** This marker reflects the glomerular filtration rate (GFR) but can be influenced by muscle mass and hydration status.
- **BUN:** Although elevated in CKD, BUN levels may be affected by diet, hydration, and protein intake.

Stages of CKD and Nutritional Interventions:

According to the IRIS classification, early stages (Stages 1 and 2) may benefit from renal diets and regular biomarker monitoring, while later stages (Stages 3 and 4) require more aggressive management - including fluid therapy, phosphorus binders, and antioxidant supplementation.[7] Renal diets (typically low in protein and restricted in phosphorus) help reduce kidney workload, and phosphorus binders are essential to prevent hyperphosphatemia. Omega-3 fatty acids may support renal function through their anti-inflammatory properties.

Biomarkers for Allergies and Gastrointestinal

Accurate allergy diagnostics rely on immune system biomarkers that can help differentiate between various allergic conditions. Some key biomarkers include:

- **IgE:** Elevated IgE levels can indicate hypersensitivity reactions and can be instrumental in diagnosing environmental or food allergies.[8]
- **Cytokines (e.g., IL-4, IL-5, IL-13):** These cytokines are integral to the allergic inflammatory process, promoting eosinophilic responses and IgE production.[9]
- **Fecal Calprotectin:** Elevated levels suggest gastrointestinal inflammation, aiding in the distinction between inflammatory bowel disease (IBD) and food intolerance.[10]

Clinical Applications and Dietary Modifications:

Based on biomarker outcomes, hypoallergenic diets using novel proteins or hydrolyzed formulations are recommended to reduce allergic responses. Dietary trials allow clinicians to monitor improvements in gastrointestinal signs, while the incorporation of probiotics supports may help a balanced gut microbiome and overall immune function.[8,9,10]

Biomarker-driven Management of Endocrine Disorders

Endocrine disorders such as diabetes, Cushing’s syndrome, and hypothyroidism are common in clinical practice. Key biomarkers for diagnosis and management include:

- **Cortisol:** Measured during ACTH stimulation or dexamethasone suppression tests, cortisol aids in diagnosing Cushing’s and Addison’s diseases.
- **T4 & TSH:** These thyroid hormones are used to diagnose thyroid disorders; low T4 with elevated TSH typically suggests hypothyroidism, while high T4 may indicate hyperthyroidism.
- **Fructosamine:** This biomarker provides an average glucose level over 2–3 weeks and is useful for monitoring diabetic patients.

Clinical Applications and Personalized Nutrition:
Integrating hormone therapies with tailored dietary modifications is essential in managing endocrine disorders. For example, low-glycemic diets help regulate blood sugar in diabetic pets, and the use of adaptogenic herbs along with omega-3 fatty acids is being explored to support patients with Cushing's disease.[4]

Cancer Biomarkers in Veterinary Medicine

Early detection of cancer through biomarkers can significantly improve treatment outcomes. Some common biomarkers include:

- **C-Reactive Protein (CRP):** As an acute-phase protein produced in response to inflammation, elevated CRP levels can signal systemic inflammation associated with malignancies.[11]
- **Thymidine Kinase 1 (TK1):** This enzyme, a marker of cellular proliferation, is elevated in several cancers - including lymphoma.[12]
- **Circulating Tumor DNA (ctDNA):** Advances in liquid biopsy technology now allow noninvasive detection of ctDNA, aiding in cancer diagnosis and monitoring.

Utilizing Cancer Biomarkers for Early Cancer Detection:
A new diagnostic screen[a] facilitates early cancer detection for companion animals. The panel is designed to identify lymphoma and other cancers before clinical signs appear.

- **Early Detection:** The test can detect cancers at an early stage, thereby improving treatment outcomes.
- **Lymphoma Detection:** It distinguishes between B-cell and T-cell phenotypes (on positive) with high sensitivity (79.3%) and specificity (98.9%).
- **Expanding Panel:** Future iterations of the test aim to include additional cancer types, broadening its diagnostic scope.
- **Integration:** Its ease of incorporation into routine wellness panels through a simple blood sample makes it a valuable tool in preventive care.

Clinical Applications and Nutritional Considerations:
Early detection allows for proactive nutritional interventions to manage cancer-related cachexia. High-protein, omega-3-enriched diets are recommended to support muscle mass and overall health during treatment, facilitating timely therapeutic interventions to alleviate pain and discomfort.[11,12]

Conclusion

Biomarkers play a transformative role in veterinary medicine by enabling early diagnosis, monitoring disease progression, and informing therapeutic strategies. In the realm of veterinary nutrition, they facilitate personalized dietary recommendations that improve metabolic health, mitigate disease progression, and enhance overall quality of life for companion animals. As research continues to advance in both biomarker discovery and precision nutrition, the future promises even more targeted and effective approaches to veterinary care.[1,2,4]

Conflicts of Interest

The author declares no conflicts of interest. Any potential conflicts related to the research or presentation content have been disclosed.

Footnote

[a] Cancer Dx: IDEXX Laboratories, Inc. (Westbrook, Maine, USA)

References

1. Freeman, L., Becvarova, I., Cave, N., MacKay, C., Nguyen, P., Rama, B., Takashima, G., Tiffin, R., van Beukelen, P., & Yathiraj, S. (2011). WSAVA nutritional assessment guidelines. *Compendium on Continuing Education for the Practicing Veterinarian, 33*(8), E1–E9.
2. Cortese, L., Terrazzano, G., & Pelagalli, A. (2019). Leptin and immunological profile in obesity and its associated diseases in dogs. *International Journal of Molecular Sciences, 20*(10), 2392. doi: 10.3390/ijms20102392
3. Montoya, M., Péron, F., Hookey, T., Morrison, J., German, A. J., Gaillard, V., & Flanagan, J. (2025). Overweight and obese body condition in dogs and cats seen at primary practices across the USA. *Preventive Veterinary Medicine, 235*, 106398. doi: 10.1016/j.prevetmed.2024.106398
4. German, A. J., Hervera, M., Hunter, L., Holden, S. L., Morris, P. J., Biourge, V., & Trayhurn, P. (2009). Improvement in insulin resistance and reduction in plasma inflammatory adipokines after weight loss in obese dogs. *Domestic Animal Endocrinology, 37*(4), 214–226. doi: 10.1016/j.domaniend.2009.07.001
5. McKenzie, B., Peloquin, M., Tovar, A., Graves, J. L., Ratcliff, E., Tucker, K., Vo, K., Greenwood, K., Halioua-Haubold, C. L., & Juarez-Salinas, D. (2024). Feeding dogs a high-fat diet induces metabolic changes similar to natural aging, including dyslipidemia, hyperinsulinemia, and peripheral insulin resistance. *American Journal of Veterinary Research, 85*(6), ajvr.23.11.0253. doi: 10.2460/ajvr.23.11.0253
6. Yerramilli, M., Farace, G., & Quinn, J. (2016). Kidney disease and the nexus of chronic kidney disease and acute kidney injury: The role of novel biomarkers as early and accurate diagnostics. *Veterinary Clinics of North America: Small Animal Practice, 46*(6), 961–993. doi: 10.1016/j.cvsm.2016.06.011
7. Segev, G., Cortellini, S., Foster, J. D., Francey, T., Langston, C., Londoño, L., Schweighauser, A., & Jepson, R. E. (2024). International Renal Interest Society best practice consensus guidelines for the diagnosis and management of acute kidney injury in cats and dogs. *The Veterinary Journal, 305*, 106068. doi: 10.1016/j.tvjl.2024.106068
8. Locher, C., Tipold, A., Welle, M., Busato, A., Zurbriggen, A., & Griot-Wenk, M. E. (2001). Quantitative assessment of mast cells and expression of IgE protein and mRNA for IgE and interleukin 4 in the gastrointestinal tract of healthy dogs and dogs with inflammatory bowel disease. *American Journal of Veterinary Research, 62*(2), 211–216. doi: 10.2460/ajvr.2001.62.211
9. Foster, A. P., Knowles, T. G., Moore, A. H., Cousins, P. D., Day, M. J., & Hall, E. J. (2003). Serum IgE and IgG responses to food antigens in normal and atopic dogs, and dogs with gastrointestinal disease. *Veterinary Immunology and Immunopathology, 92*(3–4), 113–124. doi: 10.1016/s0165-2427(03)00033-3
10. Asahina, R., & Maeda, S. (2017). A review of the roles of keratinocyte-derived cytokines and chemokines in the pathogenesis of atopic dermatitis in humans and dogs. *Veterinary Dermatology, 28*(1), 16–e5. doi: 10.1111/vde.12351
11. Malin, K., & Witkowska-Piłaszewicz, O. (2022). C-Reactive Protein as a diagnostic marker in dogs: A review. *Animals, 12*(20), 2888. doi: 10.3390/ani12202888
12. Colombe, P., Béguin, J., Benchekroun, G., & Le Roux, D. (2022). Blood biomarkers for canine cancer, from human to veterinary oncology. *Veterinary Comparative Oncology, 20*(4), 767–777. doi: 10.1111/vco.12848

Healthcare in the Age of Exponential Technology

Matthew Lungren, MD, MPH
Chief Scientific Officer, Microsoft Health & Life Sciences, Palo Alto, California, USA
mlungren@microsoft.com

Glossary of Abbreviations

AGI	artificial general intelligence
AI	artificial intelligence
GPT	generative pre-trained transformer
HIPAA	Health Insurance Portability and Accountability Act
LLM	large language models

Introduction

We are living through one of the most significant technological transformations in decades, and the impact is especially profound in healthcare. As someone who works at the intersection of academic medicine and large-scale technology, I've had a front-row seat to this shift. Much of my day-to-day involves translating healthcare needs into AI-powered solutions and identifying innovation across disciplines—from product engineering to research groups—and bringing those insights into real-world applications. This work has only grown more urgent with the rise of generative AI.

Unlocking the Future of Medical and Veterinary Care Through Generative AI

Veterinary medicine, in particular, is emerging as a surprising yet promising frontier for AI adoption. In an earlier collaboration with Dr. Diane Wilson, a veterinarian working at the forefront of AI, we proposed that veterinary professionals could lead the way in real-world AI implementation. That prediction appears to be coming true. The veterinary field shares many parallels with human medicine: workforce shortages, rising administrative burdens, and the increasing complexity of care. However, what sets veterinary care apart is a more unified ecosystem—fewer regulatory barriers, more flexible data systems, and aligned incentives to adopt innovations that immediately impact clinical efficiency. These characteristics make it fertile ground for advancing practical AI use cases.

The Evolution of AI

To understand the gravity of what's happening now, it helps to look at past technological revolutions. During an interview nearly 30 years ago, Bill Gates described the internet as a new medium that could change how we communicate, share, and access information. The skepticism then—"Isn't this just radio?"—feels strikingly similar to how many initially perceived AI. Fast-forward to today, and Gates now describes AI as the next leap: moving from a world where computing became essentially free to one where intelligence is becoming abundant and accessible. Great teaching, great medical advice—these once rare resources—are now being replicated and distributed at scale by software.

The "big bang" moment for this era came with the launch of GPT-based models. GPT-4 and its successors, particularly the newer "thinking models" like OpenAI's O1, have changed how we think about problem-solving. These models aren't optimized for dopamine-triggering engagement like many social platforms; instead, they've been adopted for their utility. GPT-based tools are now used by more than two million organizations, with over 500 million weekly active users. And these are not niche research tools—they are reshaping workflows across sectors, including healthcare.

Much of this success comes from the scaling of three ingredients: compute, data, and parameters. Together, these power the large language models (LLMs) that now seem almost intuitive in their responses. But the next leap has come from something unexpected—"test-time compute." Instead of investing exponentially more resources to retrain models, we now see that simply giving models more time to think—allowing them to reflect recursively on their outputs—can yield dramatic gains. This has major implications for medicine, where getting the right answer the first time matters.

Recent AI benchmarks, including the ARC AGI benchmark designed to test human-like problem solving, show that these thinking models outperform prior iterations, sometimes even surpassing average human performance in structured evaluations. But beyond benchmark scores, we are starting to see real-world integration. In human medicine, over 50 institutions have already deployed GPT-4 in HIPAA-compliant environments. These sandboxes allow doctors, nurses, and administrators to experiment with AI safely, gaining fluency in what these models can do while avoiding the risk of exposing patient data.

Adoption of AI in Healthcare

Surveys conducted among knowledge workers and healthcare professionals reveal widespread adoption. Two-thirds of knowledge workers report weekly use of generative AI, and in healthcare, clinicians are using these tools not only for administrative tasks but increasingly for clinical decision support. In the UK, general practitioners have used public LLMs for clinical guidance—highlighting a gap between the formal regulatory framework and the realities of frontline innovation.

The appeal is understandable. These models now perform exceptionally well on medical benchmarks. GPT-4 and its successors were not explicitly trained on healthcare data, yet they outperform purpose-built models on standardized exams like MedQA. While this raises questions about the future of medical education and licensure, it also opens doors. If models trained on general knowledge are this competent, they could play an enormous role in resource-limited settings, particularly in veterinary medicine.

Veterinary professionals face similar administrative burdens as their human health counterparts, albeit with fewer institutional supports. Streamlining documentation, client communication, and treatment planning through AI could significantly reduce burnout and increase time spent on direct care. In human healthcare, tools like ambient note-taking solutions are already proving transformative—freeing clinicians from their keyboards and allowing more eye contact with patients. A veterinary equivalent could have similarly liberating effects.

Addressing the Limitations of AI in Healthcare

Still, the text-based capabilities of AI only go so far. Most clinical information is not in text—it's in radiographs, pathology slides, and waveform data. To address this, we've been building modular AI architectures that connect specialized imaging models to general-purpose language models. Rather than retraining the entire system each time new data types are introduced, we create adapters that enable communication between different types of AI. This makes it possible to analyze a chest X-ray, detect a pneumothorax, and generate a corresponding report, all while enabling further interaction such as explaining treatment steps or flagging urgent findings.

Our open-source initiative, the AI Foundry for Health and Life Sciences, has released pretrained models for biomedical imaging—including veterinary domains—and invites researchers and clinicians to build their own applications. This approach allows partners to leverage our infrastructure while maintaining flexibility and control over their data and workflows. Some veterinary collaborators have already begun using these tools to develop imaging-based diagnostic support systems. We believe this ecosystem model—where expertise, data, and tooling are shared—will be key to scaling impactful AI solutions.

Conclusion

As we look forward, the ultimate goal is ambitious: to teach AI the full language of biomedicine. This includes understanding not only medical texts but also the patterns in genomic sequences, histopathological images, and clinical workflows. Veterinary care, with its wide variety of species, disease presentations, and settings, offers a robust proving ground for such capabilities. And because the challenges are so parallel to human medicine—yet often less encumbered by bureaucracy—the field has the potential to lead in both implementation and discovery.

We are standing at the edge of a new era in healthcare—one where intelligence is no longer the bottleneck. Whether in a rural clinic or a research hospital, the ability to access expert-level guidance in real time could become the norm. But getting there will require thoughtful implementation, domain-specific partnerships, and a willingness to reimagine what clinical practice can look like. Veterinary professionals are not only welcome participants in this journey—they may well be the ones who show us the way.

Conflicts of Interest

The author has no conflicts of interest regarding this presentation or these proceedings.

Smarter Tools, Smarter Care – Redefining Veterinary Medicine with Internet of Things (IoT), AI, and Telemedicine

Timokleia Kousi, DVM, MSc
Center for Biomedical Studies, University of BERN (Switzerland)
Timokleia.k@gmail.com

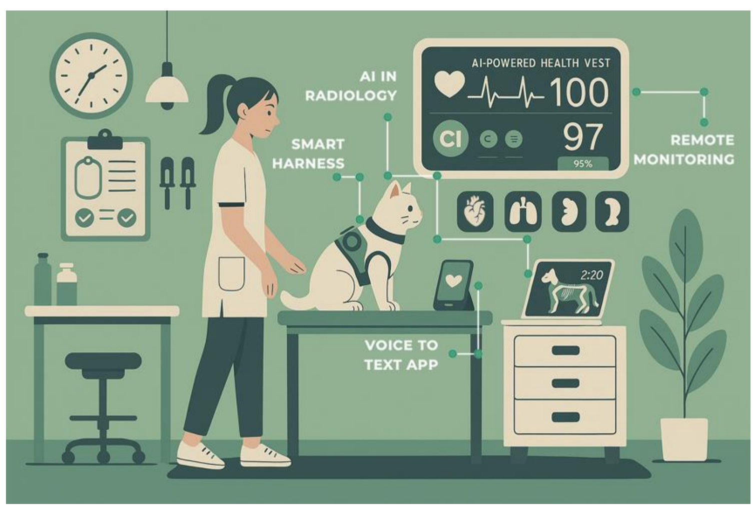
Glossary of Abbreviations

AI	artificial intelligence
DHTs	digital health technologies
DL	deep learning
IoMT	internet of medical things
IoT	internet of things
IoVT	internet of veterinary things
LLMs	large language models
ML	machine learning
M-LLMs	multimodal large language models
NLP	natural language processing
RPM	remote patient monitoring

Introduction

Veterinary medicine is undergoing a radical shift, shaped by real-time insights, smarter tools, and shifting roles. As digital health technologies[1] change how we understand, monitor, and care for animals, clinicians are now navigating a new ecosystem, where care is continuous and personalized to each patients' individual needs. This keynote explores how the integration of wearable devices, IoT, telemedicine and AI is reshaping veterinary workflows, decision-making, and client engagement. By connecting clinical challenges with technological solutions, we move toward smarter, more proactive care.

The Emerging Role of Wearables, and Internet of Things (IoT) in Veterinary Care



Across modern healthcare, **wearables and smartphones** are transforming how information flows between daily life and clinical care. Wearable technology, commonly known as "wearables," refers to small electronic devices worn directly on the body or integrated into accessories and clothing.[2] Once primarily associated with fitness tracking,[3] wearables are now recognized for their potential in remote clinical monitoring, diagnostics, and even therapeutic support.[4,5]

This growing functionality signals a shift toward a more decentralized healthcare system.[6] In veterinary medicine, wearables become essential tools for veterinary teams and pet owners alike.[7,8] By enabling real-time health monitoring outside of traditional clinical settings, veterinary wearables could promote continuous, real-time observation. Equipped with various types of sensors[5] these devices will track physiological signs remotely, delivering personalized services like medication reminders, early alerts to shifting health conditions, and timely detection of unusual behaviors. This ongoing monitoring will reduce the frequency and associated costs of physical clinic visits, while boosting remote consultations.[9,10]

Complementing this shift is the growing role of smartphones.[6] Their built-in sensors and constant connectivity make them ideal for collecting, analyzing, and relaying health data.[5] When integrated with wearables and other connected tools, they will become hubs that link veterinary patients and their caregivers to veterinary teams in real time. This ecosystem is made possible by the Internet of Things(IoT),[6] an emerging paradigm in which connected devices are embedded with sensors and network connectivity, enabling them to collect, exchange, and act on data.[8,11] In veterinary practice, IoT involves smart devices like connected collars that track activity levels, feeding stations monitoring dietary patterns, litter boxes assessing urination frequency, and room sensors detecting environmental changes. Originally used for industrial and home automation, IoT could bring similar value to veterinary clinical care: enabling observation beyond the clinic, enriching clinical data, and allowing a more continuous, responsive, and preventive model of health support.

In the veterinary setting, where patients cannot verbalize symptoms, this kind of connected intelligence is especially impactful, offering both clinicians and caregivers a clearer view of the animal's daily patterns and emerging health needs. For example, smart collars can monitor activity levels and detect subtle changes in behavior, helping identify early signs of discomfort or illness. Connected feeding stations and litter boxes provide insight into eating habits and digestive health, alerting caregivers when patterns shift. In the future, continuous glucose monitoring devices will allow vets and caregivers to closely track diabetic pets, enabling timely insulin adjustments without frequent clinic visits. Similarly, wearable ECG monitors will remotely track heart rhythms in dogs with cardiac conditions, providing early warnings of potential complications.[9] These applications illustrate how IoT and wearables create a connected ecosystem, offering veterinarians and pet owners real-time, actionable data to deliver more responsive, preventive, and individualized care.

Successfully integrating wearable technology and **Internet of Veterinary Things (IoVT)** into clinical care requires more than just the devices, it demands a thoughtful, systematic approach. Case studies from human healthcare organizations such as Kaiser Permanente and Ochsner Health[2] offer valuable lessons for veterinary medicine by highlighting key factors for successful technology implementation. Similar to human healthcare, veterinary wearables must target clearly defined clinical needs, such as managing chronic conditions in pets or monitoring postoperative recovery. These devices must integrate seamlessly into veterinary digital care systems and align with existing clinical data infrastructures.[2] Additionally, providing on-site technical support can help pet owners confidently engage with new technologies, while veterinary nurses and clinic staff can offer essential human guidance to complement digital solutions.[2] Ensuring that software interfaces are user-friendly and intuitive facilitates adoption by both veterinarians and pet owners.[2] Ultimately, clinician support and advocacy within veterinary teams are crucial for widespread adoption and sustainability, driven by tangible improvements in care efficiency and patient outcomes.

The Rise of Intelligent Assistance in Veterinary Medicine

Artificial intelligence (AI) is ushering veterinary medicine into a new era of intelligent assistance.[12] Across healthcare, AI tools are increasingly used to support clinical documentation, triage, diagnostics, and personalized care.[13] Recent expert studies forecast AI's widespread adoption across many health specialties—including pathology, radiology, and general practice.[14,15] Large Language Models (LLMs),[16] like GPT-4,[17] have expanded the capabilities of AI beyond automation, offering real-time decision support, research synthesis, and communication tools for both clinicians and clients. In the veterinary world, where patients cannot describe their symptoms, AI tools can assist in interpreting data from wearables, imaging, and lab results, helping surface meaningful insights and enhance clinical decisions.

AI Scribes : Next-Gen Medical Note Taking

As the pressure on clinicians intensifies,[18] a new kind of assistant is entering the consultation room not with a stethoscope, but with algorithms. AI scribes are being actively tested as a solution to ease clinical documentation[13] by quietly capturing conversations during visits and generating structured notes for review. Built on advances in large language models and speech recognition,[19-21] these tools aim to ease the documentation burden, reduce keyboard fatigue, and free up clinical time for more meaningful work.[22] While already gaining traction across human healthcare systems, their adoption in veterinary practice will likely follow gradually. The potential is clear. Beyond basic note generation, these systems could possibly automate the creation of referral letters, summarize patient histories, assign billing codes, and draft clear discharge instructions for pet owners. As integration with digital health records improves, these systems may quietly evolve into versatile behind-the-scenes assistants, enhancing efficiency without disrupting the clinical work at the heart of veterinary care.

AI-enhanced Clinical Decision Making

While current medical AI tools have shown promise in supporting documentation and streamlining clinical workflows, they still function largely as narrow specialists—processing single types of input like text or images.[13] For example, a model trained to detect ear infections in dogs might reliably flag inflamed tissue but wouldn't assess other possible causes of headshaking or discomfort. These narrow, task-specific systems are restricted to what they were explicitly trained for and lack the flexibility needed for broader clinical reasoning. In contrast, medical and veterinary professionals are inherently multimodal: they listen to symptoms, review lab results, examine images, and observe behaviors. To be truly helpful, AI systems must evolve to do the same.

This next frontier is represented by **multimodal large language models (MLLMs)** systems capable of simultaneously analyzing a range of data types such as clinical text, diagnostic images, sound, and video.[16,23] These models promise to go beyond single-task tools. Rather than merely identifying one condition in one image, future AI could interpret complex medical cases, offer differential diagnosis lists grounded in patient data, and support treatment plan creation with recommendations.[23] The first multimodal model that became available to the public was ChatGPT-4o from Open AI.[24]

Virtual Health Coaches

AI-powered virtual health coaches will support caregivers in managing pet health beyond the clinic by offering real-time, personalized guidance throughout recovery, chronic condition management, and everyday care.[13] Built on multimodal AI systems, these platforms will interpret inputs such as wearable data, clinical records, behavioral logs, and caregiver-reported observations. For example, a virtual health coach could help pet owners manage a dog's postoperative recovery by reminding them of medication schedules, tracking healing progress,[25] and responding promptly to unexpected changes, such as decreased activity or appetite.

By synthesizing this information, virtual coaches will deliver tailored advice on therapeutic routines, deliver timely medication reminders, and respond to caregiver questions, reducing the caregiver's reliance on vague memory or paper instructions. They will also serve as a bridge to virtual consultations, connecting caregivers directly with veterinary professionals when needed. Designed to communicate in clear, accessible language, they will help caregivers track progress, follow treatment plans, and respond to changes as they happen. This shifts home care from reactive and memory-dependent to continuous, data-driven, and proactive.

Navigating the Challenges in Implementing Digital Technologies in Veterinary Medicine

While digital innovations hold great promise for veterinary care, several significant challenges must be addressed for successful integration into clinical practice.

A primary concern is the **reliability of wearable devices**. In veterinary settings, inaccuracies in measurement can quickly undermine trust. For instance,[26] recent research revealed that commercially available canine activity trackers inaccurately estimated dogs' energy requirements, highlighting the urgent need for rigorous validation of veterinary wearables—particularly for chronic disease monitoring and clinical decision-making.

Another key challenge is the **lack of specialized veterinary AI models**, which stems directly from a critical shortage of accessible, high-quality, animal-specific datasets. Unlike human medicine, veterinary practice currently relies heavily on generalized or inadequately annotated data, limiting the possible accuracy and clinical relevance of AI tools. Developing comprehensive, well-annotated datasets covering diverse species, breeds, and conditions is essential for AI to accurately identify subtle clinical signs and provide reliable decision support in veterinary medicine.

Furthermore, the potential for **over-reliance on AI** must be carefully managed. Veterinarians and caregivers may inadvertently trust AI outputs too readily,[27] reducing vigilance or missing subtle clinical cues.[22] Clear guidelines, careful interface design, and consistent human oversight will ensure AI remains a valuable clinical assistant rather than a replacement for professional judgment.[28]

Finally, **privacy and data security** concerns are crucial.[28] There is risk of exposing sensitive client and patient data, particularly as most Large Language Model (LLM)-based solutions depend on cloud based infrastructure, increasing the potential for personal information leakage. Recent research highlights growing interest in deploying Small Language Models (SLMs), which offer efficient performance with minimal memory requirements. Data is stored directly on local devices like wearables or smartphones.[29] The veterinary profession must therefore establish strong data governance practices, including data anonymization, secure access control and exploration of privacy-preserving, to protect client confidentiality and preserve trust.

Addressing these challenges, particularly the urgent need for high-quality, veterinary-specific datasets, is essential to fully realize the transformative potential of digital tools in veterinary care.

Conclusion

Veterinary medicine is at a pivotal moment.[10] We are witnessing a global transformation toward proactive, personalized, and data-driven health management. This shift is increasingly essential, driven not only by technological advancements but also by broader demographic trends. The global pet population is rapidly growing, particularly in millennial and Gen-Z households. Simultaneously, pets are living significantly longer lives due to improved veterinary care, preventive medicine, and greater awareness of animal welfare.[30]

However, this positive trend brings its own challenges. Longer lifespans mean more chronic conditions requiring ongoing management. Veterinary practices worldwide are already feeling the strain of increasing caseloads, contributing to veterinarian shortages and mental health challenges. Many pets still lack access to adequate veterinary care, especially in regions with limited veterinary infrastructure or remote locations.[31] The shortage of qualified veterinarians and the growing pet population underscore the urgent need for scalable solutions to support veterinary professionals.[10,30]

Technology, powered by artificial intelligence (AI) presents meaningful solutions to these pressing challenges. To fully harness the potential of these technological innovations, the veterinary community must take responsibility for addressing key issues, including data privacy, clinical reliability, and the essential development of robust, animal-specific datasets. A conscious, responsible, and purposeful integration of technology into veterinary care will not only improve outcomes but also expand access, alleviating strain on veterinary teams and ensuring care reaches more animals, regardless of geography.

The future of veterinary medicine demands an interdisciplinary approach, combining veterinary expertise, technological innovation, and proactive policymaking. By embracing digital fluency, enhancing creative problem-solving skills, and advocating for supportive regulatory frameworks, veterinary professionals can actively shape a healthier, more sustainable future for animals and the humans who care for them. This is not simply a vision for the future, it is a call for action. Our collective efforts today will determine the quality of care and welfare animals receive tomorrow.

Conflicts of Interest

The author declares that she has no conflicts of interest.

References

1. Digital Therapeutics Alliance. Digital health technologies: ecosystem categorization. *DTA* (2023). https://dtxalliance.org/wp-content/uploads/2023/06/DTA_FS_DHT-Ecosystem-Categorization.pdf
2. Smuck, M., Odonkor, C. A., Wilt, J. K., Schmidt, N., & Swiernik, M. A. (2021). The emerging clinical role of wearables: factors for successful implementation in healthcare. *npj Digital Medicine, 4*, 45. doi: 10.1038/s41746-021-00418-3
3. Schumann, M., & Doherty, C. (2024). Bridging gaps in wearable technology for exercise and health professionals: a brief review. *International Journal of Sports Medicine, 45*, 949–957 (2024). doi: 10.1055/a-2376-6332
4. Smith, A.A., Li, R., & Tse, Z.T.H. (2023). Reshaping healthcare with wearable biosensors. *Scientific Reports, 13*, 4998. doi: 10.1038/s41598-022-26951-z
5. Xue, Z., Gai, Y., Wu, Y., Iiu, Z., & Li, Z. (2024). Wearable mechanical and electrochemical sensors for real-time health monitoring. *Nature Communications Materials, 5*, 211. doi: 10.1038/s43246-024-00658-2
6. Wall, C., Hetherington, V., & Godfrey, A. (2023). Beyond the clinic: the rise of wearables and smartphones in decentralising healthcare. *npj Digital Medicine, 6*, 219. doi: 10.1038/s41746-023-00971-z
7. Mitek, A., Jones, D., Newell, A., & Vitale, S. (2022). Wearable devices in veterinary health care. *Veterinary Clinics of North America: Small Animal Practice, 52*(5), 1087–1098. doi: 10.1016/j.cvsm.2022.05.001

8. Pico-Valencia, P., & Holgado-Terriza, J. A. (2025). The Internet of Things empowering the Internet of Pets—An outlook from the academic and scientific experience. *Applied Sciences, 15*(4), 1722. doi: 10.3390/app15041722
9. Teller, L. M., & Moberly, H. K. (2020). Veterinary telemedicine: A literature review. *Veterinary Evidence, 5*(4). doi: 10.18849/ve.v5i4.349
10. Telemedicine. (2024). *Vet Times*. Available at: https://www.vettimes.com/news/business/sustainability/telemedicine
11. The Medical Futurist. (2019). A Digitally Caring Environment: The Internet of Things in Hospitals. Available at: https://medicalfuturist.com/iot-in-hospitals
12. Topol, E. J. (2019). High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine, 25*, 44–56 (2019). doi: 10.1038/s41591-018-0300-7
13. Moor, M., Banerjee, O., Abad, Z.S.H., Krumholz, H. M., Leskovec, J., Topol, E. J., & Rajpurkar, P. (2023).. Foundation models for generalist medical artificial intelligence. *Nature, 616*, 259–265. doi: 10.1038/s41586-023-05881-4
14. Blease, C., Kharko, A., Locher, C., DesRoches, C. M., & Mandl, K. D. (2020). US primary care in 2029: a Delphi survey on the impact of machine learning. *PLoS ONE,* 15, e0239947. doi: 10.1371/journal.pone.0239947
15. Berbís, M. A.. McClintock, D. S., Bychkov, A., Van der Laak, J., Pantanowitz, L., Lennerz, J. K., …Shen, J. (2023). Computational pathology in 2030: a Delphi study forecasting the role of AI in pathology within the next decade. *eBioMedicine, 88*, 104427. doi: 10.1016/j.ebiom.2022.104427
16. Meskó, B., & Görög, M. (2023). The impact of multimodal large language models on health care's future. *Journal of Medical Internet Research, 25*, e52865 (2023). doi: 10.2196/52865
17. OpenAI. Introducing ChatGPT. *OpenAI* (2024). https://openai.com/index/chatgpt/
18. Misurac, J., Knake, L. A., & Blum, J. M. (2025). The effect of ambient artificial intelligence notes on provider burnout. *Applied Clinical Informatics, 16*(2), 252-258. doi: 10.1055/a-2461-4576
19. Dorn, S. (2024). Where healthcare AI ambient scribes are heading. *Forbes*. Available at: https://www.forbes.com/sites/spencerdorn/2024/11/15/where-ai-ambient-scribes-are-heading/
20. From Dictation to Automation: The Rise of AI Scribes in Healthcare. *RCP Medical Care*. Available at : https://medicalcare.rcp.ac.uk/content-items/blog/from-dictation-to-automation-the-rise-of-ai-scribes-in-healthcare/
21. The Medical Futurist. (2024). Voice to text technologies shape the future of electronic medical records. Available at: https://medicalfuturist.com/voice-to-text-technologies-shape-the-future/
22. Tierney, A. A., Gayre, G., Hoberman, B., Mattern, B., Ballesca, M., Kipnis, P., Liu, V., & Lee, K. (2024). Ambient artificial intelligence scribes to alleviate the burden of clinical documentation. *NEJM Catalyst, 5*(3). doi: 10.1056/CAT.23.0404
23. Rao, V.M., Hla, M., Moor, M., Adithan, S., Kwak, S., Topol, E. J., & Rajpurkar, P. (2025). Multimodal generative AI for medical image interpretation. *Nature, 639*, 888–896. doi: 10.1038/s41586-025-08675-y
24. Open AI. (2024). Hello GPT-4o. Available at: https://openai.com/index/hello-gpt-4o/
25. Meng, L., Liu, S., Borsa, B.A., Eriksson, M., & Mak, W. C. (2024). A conducting polymer-based array with multiplex sensing and drug delivery capabilities for smart bandages. *Nature Communications Materials, 5*, 28. doi: 10.1038/s43246-024-00469-5
26. Sekhar, M., Rudinsky, A. J., Cashman, C., Parker, V. J., Kieves, N. R., Howard, J., & Winston, J. (2024). Commercially available wearable health monitor in dogs is unreliable for tracking energy intake and expenditure. *American Journal of Veterinary Research*, *85*(3). doi: 10.2460/ajvr.23.10.0242
27. Lee, P., Bubeck, S., & Petro, J. Benefits, limits, and risks of GPT-4 as an AI chatbot for medicine. *New England Journal of Medicine, 388*(13), 1233–1239. doi: 10.1056/NEJMsr2214184
28. Meskó, B., & Topol, E.J. (2023). The imperative for regulatory oversight of large language models (or generative AI) in healthcare. *npj Digital Medicine,* **6**, 120. doi: 10.1038/s41746-023-00873-0
29. Wang, X., Dang, T., Kostakos, V., & Jia, H. (2024). Efficient and personalized mobile health event prediction via small language models. In Proceedings of the 30th Annual International Conference on Mobile Computing and Networking, 2353-2358. New York, NY. Association for Computing Machinery. doi: 10.1145/3636534.3698123
30. Global Animal Health Association. (2022). Global State of Pet Care. Available at: https://healthforanimals.org/reports/pet-care-report/global-state-of-pet-care/.
31. Walter, J. R., Xu, S., & Rogers, J. A. (2024). From lab to life: How wearable devices can improve health equity. *Nature Communications, 15*, 123. doi: 10.1038/s41467-023-44634-9

Flowers for Algorithm: AI & Veterinary Radiology

Eli B. Cohen, DVM, DACVR
Dragonfly Imaging, Cary, NC, USA
NC State College of Veterinary Medicine, Raleigh, NC, USA
ecohen@dragonflyimaging.vet

Glossary of Abbreviations

AI	artificial intelligence
AVMA	American Veterinary Medical Association
BP	best practice
DL	deep learning
FDA	Food & Drug Administration
GMLP	good machine learning practices
GPT	generative pre-trained transformers
LLM	large language models
ML	machine learning
NLP	natural language processing
SaMD	software as a medical device
SOC	standard of care
VCPR	veterinary-client patient relationship

Introduction

Artificial intelligence (AI) is an overarching term encompassing algorithmic computer emulation of human intelligence and decision making. Within AI, there are multiple subsets including but not limited to machine learning (ML), deep learning (DL), natural language processing (NLP), large language models (LLM), and generative pre-trained transformers (GPT). As a rapidly developing and disruptive technology, the types and uses of AI will continue to grow. In all aspects of life including veterinary radiology and consulting, AI will be both a disruptive and a layering technology. It will bring about new solutions and workflows that have not previously been present, but as a layering technology, it will become integrated in most if not all current workflows as well. There are key differences in veterinary medicine from human medicine which will require us to consider additional safeguards and guardrails while facilitating adoption of this rapidly changing technology.

Impacts of AI

AI will impact all components of veterinary radiology/imaging and veterinary consulting, and this talk will outline a potential vision of AI augmented workflows. This will be from the perspective of product offerings/solutions currently on the market, as well as emerging and potential product/solutions.

Supercharged Pet Parents

AI and assisted technologies will allow pet parents increased access to information tailored for their pet, the ability to sequentially monitor and record physiologic parameters of their pet, assess problems and triage need for veterinary care as they arise, and to have the entirety of their pet's medical record at their fingers and to provide to either their primary veterinarian or during an emergency/referral/new practice visits.

Supercharged Pet Visits

Technologies will allow identification of patient's as they walk through the door, streamlining visits and autopopulating/updating patient records from pet parent files and real-time data. This will allow for more informed pet owners to provide more complete and higher quality information to the veterinary medical staff, allowing for more efficient and accurate diagnosis and treatment planning. Technologies including AI powered NLP will be leveraged to record medical histories and populate patient records, allowing veterinarians to practice more doctoring and less time with monotonous repetitive tasks. Veterinarians will need to consider how to manage quality control of these new technologies to ensure that recorded in auto populated records are accurate and error free.

Veterinary Efficiency

AI powered NLP will allow offloading of some monotonous medical records, but will also be used to generate submission forms and paperwork for outside consulting including radiologist consults for image assessment. This will allow the treating veterinarians and their staff to spend less time completing paperwork, and will also increase the completeness and accuracy of submission forms to support services including radiology, clinical pathology, pathology, etc. This technology will also be used to create submissions for referral ensuring continuity of medical record between facilities.

Quality Control/Safety

AI will be integrated in point-of-care image acquisition. This may provide guidance in what images and views to acquire, as well as quality control to ensure that acquired images have diagnostic imaging and positioning, as well as assessment for any radiation safety errors with cues to the staff onsite. This will not only increase efficiency at time of acquisition, reducing radiation to staff and patient and potentially cost to the client, but also optimizing the quality of diagnostic images for subsequent consultation increasing efficiency and accuracy for imaging consultants (as well as onsite interpretation). This will be a key component in allowing radiologists to be more efficient, potentially lowering costs and increasing access to radiologist assessment, moving us towards a new standard of care (SOC) closer to that of our human counterparts.

AI Diagnosis

Once properly validated according to good machine learning practices (GMLP) and standards provided by relevant domain experts, AI can be used as part of the clinical decision making chain. If done properly, this will increase human efficiency, increase accuracy/reduce errors, and also offload repetitive monotonous tasks to allow humans to spend more of their time interpreting and synthesizing complex information to improve patient care. If done hastily or improperly without appropriate validation, this has potential to cause serious patient harm, particularly given our ability to perform euthanasia when indicated. In consideration of integration of AI diagnostic aids, it is imperative to have a strong understanding of human cognitive biases and how they could be exacerbated by AI diagnostic aids, in particular concepts of premature closure, satisfaction of search, diagnostic momentum, and automation bias. As has been developed in human medicine, it will be important for us in veterinary medicine to consider AI/AI products through the scope of risk stratification, with greater guidelines and guardrails for those products that have potential to cause greater risk in patients. Until proven otherwise, best practice should be considered AI with a human (domain expert) in the loop particularly in clinical diagnostic decision making.

AI Research

AI has potential to increase efficiency and discovery in veterinary imaging research, including facilitating discovery of patterns that may not be apparent to human assessment.

AI Teaching

For many years there has been a drain of veterinary radiologists from academia, which is where the lion's share of training a veterinary radiologists occurs. For this reason in conjunction with market forces between private practice and academia, there are some veterinary institutions that have no veterinary radiologists or minimal staffing. AI has the potential to increase access to domain expert level knowledge to institutions which do not otherwise have a radiologist on staff. AI will also be used as personal tutors not only in veterinary radiology, but in all domains of the veterinary curriculum. As such, it is imperative that these technologies are properly validated to ensure that disseminate information is accurate and defensible.

AI Regulation

Software is a medical device (SaMD) is a relatively new category of medical device which comprises the majority of AI offerings. While AI/SaMD is subject to premarket approval by the FDA for human devices, this is not the case in veterinary medicine where there is a loophole. There are no requirements for FDA premarket approval of medical devices (including SaMD) in veterinary medicine. While this may be viewed by some as an avenue to allow accelerated development and adoption of AI/SaMD in veterinary medicine, it raises clear issues of properly validated products that will not cause harm to patients. In the absence of any regulation, we are reliant on companies to ethically develop properly validated products, and end-users (who typically will not be domain experts) to assess products when they may not be provided the information necessary to make such appraisals. This raises key issues of transparency from AI/SaMD, and would necessitate these entities adopting GMLP without any requirement to do so. Beyond that, AI will raise key issues in regards to the VCPR (in particular whether AI can hold one), and whether AI can or should be seen as a consultant or referral in the context of the AVMA Principles of Medical Ethics. New principles will likely be needed to properly address and encompass the roles and uses of AI including SaMD.

Conclusion

AI will have many predictable and likely some unpredictable impacts in veterinary radiology and consulting. This technology will affect all facets of the profession, as well as supercharging pet parents. If deployed ethically and responsibly, we will see improvements in information access, information accuracy, streamlined veterinary visits, improved diagnostics and quality control, diagnostic aids, increased access to domain experts, scientific discovery, and training. If deployed hastily and unethically, it has potential to cause harm to our patients and their pet parents, degrade our critical thinking abilities, and erode trust and adoption. A concerted collaborative effort should be placed on developing necessary guardrails for safety and accuracy, including rethinking veterinary practice guidelines in the context of this emerging technology.

Conflicts of Interest

Owner/Radiologist – Dragonfly Imaging
Adjunct Professor – NC State College of Veterinary Medicine
Consultant – Daisy A.I.
Member – ACVR subcommittee on A.I.
Member – AVMA Task Force on Emerging Technologies and Innovation

References

1. American Veterinary Medical Association. (2019). AVMA Policies- *Principles of Veterinary Medical Ethics of the AVMA*. Accessed January 1, 2022; https://www.avma.org/resources-tools/avma-policies/principles-veterinary-medical-ethics-avma
2. American Veterinary Medical Association. AVMA Policies-Veterinarian's Oath. Accessed January 1, 2022; https://www.avma.org/resources-tools/avma-policies/veterinarians-oath.
3. American Veterinary Medical Association. The Veterinarian-Client-Patient-Relationship. Accessed January 1, 2022; https://www.avma.org/resources-tools/pet-owners/petcare/veterinarian-client-patient-relationship-vcpr
4. Anderson, A., & Anderson, S. L. (2019). How should AI be developed, validated, and implemented in patient care? *AMA Journal of Ethics*, *21*(2), E125-130. doi: 10.1001/amajethics.2019.125
5. Block, G. (2018). A new look at standard of care. *Journal of the American Veterinary Medical Association*, 252(11), 1343-1344. doi: 10.2460/javma.252.11.1343
6. Brady, A. P., & Neri, E. (2020). Artificial intelligence in radiology-ethical considerations. *Diagnostics*, *10*, 231. doi: 10.3390/diagnostics10040231
7. Castelvecchi, D. (2016). Can we open the black box of AI? *Nature*, *538*(7623), 20-23. doi: 10.1038/538020a
8. Cohen, E. B., & Gordon, I. K. (2022). First, do no harm. Ethical and legal issues of artificial intelligence and machine learning in veterinary radiology and radiation oncology. *Veterinary Radiology & Ultrasound, 63*(S1), 840-850. doi: 10.1111/vru.13171
9. Cohen, I.G. (2020). Informed consent and medical artificial intelligence: What to tell the patient? *The Georgetown Law Journal*, *108*, 1425
10. Dyess v Caraway, 190 SO 2d 666, La 1966.
11. Erickson, B. J. Korfiatis, P. Akkus, Z. & Kline, T. L. (2017). Machine learning for medical imaging. *Radiographics*, *37*(2), 505–515. doi: 10.1148/rg.2017160130
12. Forti, M. (2021). The deployment of artificial intelligence tools in the health sector: Privacy concerns and regulatory answers with the GDPR. *European Journal of Legal Studies*, *13*, 1. doi:10.2924/EJLS.2019.040
13. Geis, J. R., Brady, A., Wu, C. C., Spencer, J., Ranschaert, E., Jaremko, J. L., Langer, S. G., ...Kohli, M. (2019). Ethics of artificial intelligence in radiology: summary of the joint European and North American multisociety statement. *Insights into Imaging*, *10*,101. doi: 10.1186/s13244-019-0785-8
14. Gerke, S., Minssen, T., & Cohen, G. (2020). Ethical and legal challenges of artificial intelligence-driven healthcare. In Bohr, A., & Memarzadeh, K., (Eds.) *Artificial Intelligence in Healthcare*, (pp. 295-336). Elsevier. doi: 10.1016/B978-0-12-818438-7.00012-5
15. Hood, C. R., & Derosier, J. M. (2016). How to perform a root cause analysis for workup and future prevention of medical errors: a review. *Patient Safety in Surgery,* 10, 20. doi: 10.1186/s13037-016-0107-8
16. International Medical Device Regulators Forum. (2014). "Software as a medical device": Possible framework risk categorization and corresponding considerations. https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf
17. International Medical Device Regulators Forum. (2025). Good machine learning practice for medical device development: Guiding principles. Artificial Intelligence/Machine Learning-enabled Working Group. https://www.imdrf.org/consultations/good-machine-learning-practice-medical-device-development-guiding-principles
18. Jaremko, J.L., Azar, M., Bromwich, R., Lum, A., Cheong, L. H. A., Gibert, M., Laviolette, F., ...Canadian Association of Radiologists (CAR) Artificial Intelligence Working Group. (2019). Canadian Association of Radiologists white paper on ethical and legal issues related to artificial intelligence in radiology. *Canadian Association of Radiologists, 70*(2), 107-118. doi: 10.1016/j.carj.2019.03.001
19. Kohil, M., Prevedello, L. M. Ross, F. W. & Geis, J. R. (2017). Implementing machine learning in radiology practice and research. *American Journal of Roentgenology*, *208*(4), 754-760. doi: 10.2214/AJR.16.17224
20. Kundu, S. (2021). AI in medicine must be explainable. *Nature Medicine*, *27*(8), 1328. doi: 10.1038/s41591-021-01461-z
21. Lakhani, P., Prater, A. B., Hutson, R. K., Andriole, K. P., Dreyer, K. J., Morey, J., ...Hawkins, C. M. (2018). Machine learning in radiology: Applications beyond image interpretations *Journal of the American College of Radiology, 15*(2), 350-359. doi: 10.1016/j.jacr.2017.09.044
22. Liew, C. (2018). The future of radiology augmented with artificial intelligence: A strategy for success. *European Journal of Radiology*, *102*, 152-156. doi: 10.1016/j.ejrad.2018.03.019

23. Lim, S. S., Phan, T. D. Law, M., Goh, G. S., Moriarty, H. K., Lukies, M. W., Joseph, T., & Clements, W. (2022). Non-radiologist perception of the use of artificial intelligence (AI) in diagnostic medical imaging reports. *Journal of Medical Imaging and Radiation Oncology, 66(*8), 1029-1034. doi: 10.1111/1754-9485.13388
24. Medical Device Coordination Group. (2019). Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR. https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2019_11_guidance_qualification_classification_software_en_0.pdf
25. Mudgal, K. S., & Das, N. (2020). The ethical adoption of artificial intelligence in radiology. *BJR Open*, *2*(1), 20190020. doi: 10.1259/bjro.20190020
26. Nencka, A.S. (2020). Editorial for "Top 10 reviewer critiques of radiology artificial intelligence (AI) articles: Qualitative thematic analysis of reviewer critiques of machine learning/deep learning manuscripts submitted to JMRI". *Journal of Magnetic Resonance Imaging*, 52(1), 255-256. doi :10.1002/jmri.27054
27. RenAIssance Foundation. The Call – Ethics. Accessed January 1, 2022. http://romecall.org.
28. Siau, K., & Wang, W. (2020). Artificial intelligence (AI) ethics: Ethics of AI and ethical AI. *Journal of Database Management, 31*(2), 74-87. doi: 10.4018/JDM.2020040105
29. Tang, A., Tam, R., Cadrin-Chenevert, A., Guest, W., Chong, J., Barfett, J., Chepelev, L., …Geis, R. (2018). Canadian Association of Radiologists white paper on artificial intelligence in radiology. *Canadian Association of Radiologists Journal*, *69*(2), 120-135. doi: 10.1016/j.carj.2018.02.002
30. Tannenbaum, J. (1995). Benefits and burdens: Legal and ethical issues raised by veterinary specialization. *Advances in Veterinary Science and Comparative Medicine*, *39*, 253-296. doi: 10.1016/s0065-3519(06)80021-2
31. U.S Food & Drug Administration. Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)- Based Software as a Medical Device (SaMD) . 2020. Accessed April 1, 2022. https://www.fda.gov/media/122535/download
32. United States Food & Drug Administration. How FDA Regulates Animal Devices. Accessed January 1, 2022. https://www.fda.gov/animal-veterinary/animal-health-literacy/how-fda-regulates-animal-devices

The Impact of AI on Veterinary Diagnostics and Consulting

Candice Chu, DVM, PhD, DACVP
Assistant Professor, Department of Veterinary Pathobiology, Texas A&M University (USA)
cchu@cvm.tamu.edu

Glossary of Abbreviations

AI	artificial intelligence
CNN	convolutional neural networks
DL	deep learning
nRBC	nucleated red blood cells

Introduction

Artificial Intelligence (AI) has rapidly emerged as a transformative tool in veterinary medicine, particularly for veterinary clinical pathology. New AI-driven technologies have been developed to assist with diagnostic tasks such as hematology and cytology. This review summarizes recent developments in AI for veterinary hematology and cytology, highlights commercial products and research initiatives. The aim is to provide a practical overview for veterinarians who wish to incorporate or better understand AI-driven diagnostic tools in their clinics.

Applications of AI in Hematology

AI has the potential to automate blood smear evaluation. A recent study used deep learning (DL) convolutional neural networks (CNN) for canine and feline blood smears.[1] The algorithm was tested against board-certified clinical pathologists for tasks like leukocyte differential counts, platelet estimates, and reticulocyte (polychromatophil) identification. The results were promising: the five-part leukocyte differential by the AI agreed with pathologists 96.6% of the time in dogs and 91.7% in cats, platelet clumps were detected with ~90% sensitivity, and reticulocyte identification reached 100% agreement with experts.

One commercial platform[a] now includes an AI Blood Smear application that provides an in-clinic blood cell analysis to supplement CBC data. The AI Blood Smear algorithm includes a WBC differential count, AI estimated platelet count and platelet clumps, and AI identifies and counts polychromatophils and nucleated red blood cells (nRBC).

Another commercially available analyzer[b] provides automated morphologic assessment, including platelets, spherocytes, red blood cell agglutination, and immature neutrophils, with integration with hematology reports from connected analyzers.[c] The manufacturer claims that the deep AI learning models have been trained by board-certified pathologists using tens of thousands of patient samples.

In practice, AI hematology applications can reduce the need for manual smear reviews except for flagged cases. In the future, detection of subtle morphologic changes (e.g. toxic neutrophils, blood parasites) using AI might be expected, which will assist general practitioners in making timely diagnoses.

Applications of AI in Cytology

Digital cytology refers to scanning microscope slides into high-resolution digital images for analysis. In the last few years, in-clinic digital slide scanners have been deployed by veterinary labs[a,b,c] to connect clinics with pathologists. These digital cytology products emphasize 24/7 service with same-day report delivery. While digital cytology itself is not AI, it lays the groundwork by creating the digital image data on which AI algorithms can be trained.

In January 2025, an AI-based cytologic analysis[e] for in-clinic screening of common lymph node and subcutaneous mass aspirates for potential neoplastic cells.[2] AI Masses is expected to launch in the United States in the second quarter of 2025. A competitor[b] also plans to launch cytology support in the near future.

Multiple studies have highlighted the potential of AI in cytologic interpretation. One research group employed RetinaNet, a convolutional neural network (CNN)-based object detection algorithm[3] optimized for identifying small objects, to quantify hemosiderophages and generate total hemosiderin scores in bronchoalveolar lavage fluid from horses with exercise-induced pulmonary hemorrhage.[4,5] The algorithm achieved an accuracy of 92.3% and demonstrated strong concordance with a reference dataset annotated by 10 independent evaluators.[4] In canine cytology, two studies have explored the application of CNNs to distinguish among neoplastic, inflammatory, and hyperplastic skin lesions, as well as to classify three types of round cell tumors—lymphoma, histiocytoma, and mastocytoma—based on cytologic images from cutaneous lesions.[6,7]

For general practitioners, the combination of digital cytology (rapid access to specialists) and AI pre-screening (immediate in-house insights) can significantly improve diagnostic confidence and patient care in cytology cases.

Conclusion

In conclusion, the integration of artificial intelligence into veterinary clinical pathology is already in progress and poised for further expansion. This technology offers significant advantages in terms of diagnostic speed and comparable accuracy. However, rigorous validation studies, standardization protocols, and ethical guidelines must be carefully established to realize AI's full potential in veterinary hematology and cytology. Successfully addressing these challenges will allow AI to become an invaluable adjunct in veterinary laboratories, amplifying the skills of veterinarians and pathologists while preserving their essential roles in clinical reasoning, critical analysis, and compassionate patient care.

Conflicts of Interest

The author is a paid speaker by IDEXX at AVMA, VMX, and IDEXX webinars.

Footnotes:

a Vetscan Imagyst: Zoetis Services, LLC (Parsippany, New Jersey, USA)
b InVue DX Cellular Analyzer: IDEXX Laboratories, Inc. (Westbrook, Maine, USA)
c ProCyte One, ProCyte DX Analyzers: IDEXX Laboratories, Inc. (Westbrook, Maine,USA)
d HeskaView: Antech Diagnostics, Inc. (Fountain Valley, California, USA)
e AI Masses for Vetscan Imagyst: Zoetis Services, LLC (Parsippany, New Jersey, USA)

References

1. Morissette, E. *et al.* Point-of-care platform integrated with deep-learning, convolutional neural network algorithms effectively evaluates canine and feline peripheral blood smears. *Am J Vet Res* 1–11 (2024) doi: 10.2460/ajvr.24.08.0226.
2. New AI tool for in-clinic cancer screening is announced. (2025). *DVM 360* https://www.dvm360.com/view/new-ai-tool-for-in-clinic-cancer-screening-is-announced

3. Lin, T.-Y., Goyal, P., Girshick, R., He, K. & Dollár, P. Focal loss for dense object detection. in *Proceedings of the IEEE International Conference on Computer Vision (ICCV)* (2020). doi:10.1109/TPAMI.2018.2858826.
4. Bertram, C. A., Marzahl, C., Bartel, A., Stayt, J., Bonsembiante, F., Beeler-Marfisi, J., Barton, A. K., ...Hill, J. (2023). Cytologic scoring of equine exercise-induced pulmonary hemorrhage: Performance of human experts and a deep learning-based algorithm. *Veterinary Pathology, 60*(1), 75–85. doi: 10.1177/03009858221137582
5. Marzahl, C., Aubreville, M., Bertram, C. A., Stayt, J., Jasensky, A.-K., Bartenschlager, F., Fragoso-Garcia, M., ...Maier, A. (2020). Deep learning-based quantification of pulmonary hemosiderophages in cytology slides. *Scientific Reports, 10*(1), 9795. doi: 10.1038/s41598-020-65958-2
6. Caputa, J., Łukasik, D., Wielgosz, M., Karwatowski, M., Frączek, R., Russek, P., & Wiatr, K. (2021). Fast pre-diagnosis of neoplastic changes in cytology images using machine learning. *Applied Sciences, 11*(16), 7181. doi: 10.3390/app11167181
7. Zapata, L., Chalco, L., Aguilar, L., Pimbosa, E., Ramírez-Morales, I., Hidalgo, J., Yandun, M., Arias-Flores, H., Guevara, C., & Ahram, T. (2020). Detection of cutaneous tumors in dogs using deep learning techniques. In *Advances in Artificial Intelligence, Software and Systems Engineering* (pp. 83–91). Springer International Publishing, Cham. doi: 10.1007/978-3-030-20454-9_8

Human Bonding, the Future of AGI, and Robotic/Biomimetic Pets: Should We be Worried?

Patrick Flynn, DVM, MS (Anthrozoology)
Tampa, Florida
Patrick.Flynn@zoetis.com

Glossary of Abbreviations

AGI	artificial general intelligence
AI	artificial intelligence

Introduction

The concept of robotic pets has transitioned from the realm of science fiction to a tangible reality, with advancements in artificial intelligence (AI) and robotics making these mechanical companions increasingly sophisticated and lifelike. Robotic pets offer numerous potential benefits, including companionship without the responsibilities associated with living animals, therapeutic applications, and accessibility for individuals with allergies or physical limitations. However, the debate continues on whether these AI-driven entities can truly replace the emotional and psychological bonds formed with real pets. This essay explores the potential of robotic pets, examining their advantages, limitations, and most importantly, looks at the neurochemistry and social behavior of how humans bond.

First Off, what is AI vs AGI?

Simply, it's the difference between a system designed to handle various tasks versus an entity that can think on its own and even generate its own ideas.

Artificial Intelligence (AI) refers to the broad field of computer science dedicated to creating systems capable of performing tasks that typically require human intelligence. These tasks include learning, reasoning, problem-solving, perception, and language understanding. AI systems are designed to handle specific tasks and are often categorized as narrow AI or weak AI because they operate within a limited domain. Examples include virtual assistants like Siri and Alexa, recommendation algorithms used by Netflix and Amazon, and autonomous vehicles. These systems rely on large datasets and sophisticated algorithms to identify patterns and make decisions, but they do not possess general cognitive abilities.

Artificial General Intelligence (AGI), on the other hand, represents a more advanced and theoretical stage of AI development. AGI refers to machines that possess the ability to understand, learn, and apply knowledge across a wide range of tasks at a level comparable to human intelligence. Unlike narrow AI, AGI would be capable of performing any intellectual task that a human can, including abstract thinking, creativity, and emotional understanding. The development of AGI remains a significant challenge and is the subject of ongoing research and debate within the AI community. Achieving AGI would require breakthroughs in areas such as machine learning, cognitive science, and neuroscience, and it raises important ethical and societal questions about the future of human-machine interaction, particularly in the realm of pets. Imagine an AGI that is completely autonomous and behaves and even moves exactly like a living dog, is soft and warm and can think on its own.

How Could a Human Bond with a Non-living Thing, and What is Neoteny?

Neoteny refers to the retention of juvenile features in the adult stage of an organism. In humans, neoteny manifests in physical traits such as a relatively large head, flat face, and large eyes, as well as behavioral traits like curiosity and playfulness

These traits are thought to play a significant role in human bonding.

1. **Physical Traits**: The juvenile features retained in adults, such as large eyes and expressive faces, can evoke nurturing responses from others, facilitating bonding.
2. **Behavioral Traits:** Playfulness and curiosity as well as other traits associated with neoteny, encourage social interactions and shared activities, strengthening bonds.
3. **Can Be Manipulated in Sales:** Images using neoteny are used to generate sales in everything from car design to dolls. The magic word that humans say when they are influenced by neoteny is “cute”.

Bonding with Non-living Things

Humans often form emotional attachments to non-living things, such as pets, toys, or even objects like cars. This phenomenon can be explained through several mechanisms:

1. **Anthropomorphism:** Humans tend to attribute human-like characteristics to non-living things, making them seem more relatable and easier to bond with
2. **Neotenous Features:** Many non-living things, especially toys and pets, are designed with neotenous features that evoke nurturing responses.
3. Emotional Support: Non-living things can provide comfort and a sense of security, like human relationships can.

Bonding with Dogs

Dogs, although living beings, often exhibit neotenous traits that enhance bonding with humans:

1. Physical Appearance: Dogs have features like large eyes and playful behavior that trigger nurturing instincts in humans.
2. Behavioral Traits: Dogs' loyalty, playfulness, and dependency on humans foster strong emotional bonds.
3. Companionship: Dogs provide emotional support, companionship, and a sense of purpose, like human relationships

Role of Neoteny in Human Bonding

Neoteny plays a crucial role in human bonding by evoking nurturing responses and facilitating social interactions. This concept extends to bonding with non-living things and pets, where neotenous traits and anthropomorphism enhance emotional connections. Understanding these mechanisms can provide insights into the nature of human relationships and attachments and potentially, if done accurately, could be a pathway to convincing people that a biomimetic pet is a reasonable facsimile for a living pet.

Advantages of Robotic Pets

Companionship Without the Hassle

One of the primary advantages of robotic pets is the companionship they offer without the associated maintenance and responsibilities of living animals. Traditional pets require feeding, grooming, veterinary care, and exercise, which can be time-consuming and costly. In contrast, robotic pets do not need food, medical attention, or physical exercise, making them an attractive option for individuals with busy lifestyles or limited physical capabilities. Populations living in large cities who are not able to have traditional pets may be most interested in the possibility of having a dog or cat without all the difficulties of having a living pet.

Hypoallergenic and Clean

Robotic pets are hypoallergenic, making them suitable for individuals who suffer from allergies to pet dander. This inclusivity allows more people to enjoy the benefits of pet companionship without the risk of allergic reactions. Additionally, robotic pets do not shed fur or produce waste, contributing to a cleaner living environment. Imagine being able to select your pet's coat and what it is made of so that the chance of allergies is minimized.

Therapeutic Applications

Robotic pets have shown promise in therapeutic settings, particularly for the elderly and individuals with cognitive impairments such as dementia. Studies have indicated that interaction with robotic pets can reduce feelings of loneliness, anxiety, and depression among elderly residents in care facilities. These mechanical companions can provide a sense of purpose and routine, which is beneficial for mental health.

Educational Tools

For children, robotic pets can serve as educational tools, teaching them about responsibility and empathy without the risk of harm to a living animal. These pets can be programmed to simulate various behaviors, providing a safe and controlled environment for children to learn about pet care.

Limitations of Robotic Pets

Lack of Genuine Emotional Connection

Despite their lifelike appearances and behaviors, robotic pets lack the genuine emotional connection that living animals provide. Real pets exhibit spontaneous and unpredictable behaviors, forming unique bonds with their owners. The absence of true emotions in robotic pets can be a significant drawback for individuals seeking a deep, emotional relationship with their companion.

Limited Interaction and Learning

While advanced AI allows robotic pets to mimic certain behaviors and respond to commands, their interactions are still limited compared to those of living animals. Real pets can learn from their environment and experiences, displaying a wide range of behaviors and emotions. Robotic pets, on the other hand, operate within the constraints of their programming, which could limit the depth and variety of interactions.

Ethical and Psychological Concerns

The rise of robotic pets also raises ethical and psychological concerns. Some argue that relying on robotic pets for companionship may lead to further isolation and a decrease in human-to-human interactions. Additionally, there are concerns about the potential for individuals to form unhealthy attachments to robotic pets, blurring the lines between reality and artificiality.

The Future

Technological Advancements

As technology continues to advance, the capabilities of robotic pets are expected to improve significantly. Future iterations may feature more sophisticated AI, allowing for more complex interactions and learning abilities. Enhanced sensory inputs, such as touch and sound, could make robotic pets even more lifelike, further bridging the gap between artificial and real companionship.

Integration with Smart Home Systems

Robotic pets could also be integrated with smart home systems, providing additional functionalities beyond companionship. For example, they could assist with home security, monitor the health and well-being of their owners, and even perform household tasks. This multifunctionality could make robotic pets an integral part of modern smart homes. They may also be able to be a form of ChatGPT and answer your random questions about any topic.

Broader Acceptance and Accessibility

As societal attitudes towards technology and AI evolve, the acceptance of robotic pets is likely to increase. With continued research and development, these mechanical companions could become more affordable and accessible, making them a viable option for a broader range of individuals. This increased accessibility could enhance the quality of life for many, particularly those who are unable to care for traditional pets.

Conclusion

Robotic pets hold significant potential as companions, therapeutic tools, and educational aids. Their advantages, such as low maintenance, hypoallergenic properties, and therapeutic benefits, make them an attractive alternative to traditional pets. However, the limitations, including the lack of genuine emotional connection and limited interaction capabilities, must be acknowledged. As technology advances, the future of robotic pets looks promising, with the potential for more sophisticated and lifelike companions. Ultimately, while robotic pets may not fully replace the emotional bonds formed with living animals, they offer a valuable and complementary option for those seeking companionship and support.

Conflicts of Interest

The author has no conflicts of interest regarding this presentation or these proceedings.

References

1. BiologyInsights Team. (2025, February 8). *Living and nonliving things interacting in an environment: How they coexist*. https://biologyinsights.com/living-and-nonliving-things-interacting-in-an-environment-how-they-coexist/
2. England, A. (2025, February 17). Could robot pets be the future? Here's what the experts are predicting. PetsRadar. https://www.petsradar.com/news/could-robot-pets-become-popular-in-the-future
3. Hazan, C., & Campa, M. I. (Eds.). (2013). *Human bonding: The science of affectional ties*. The Guilford Press.
4. Kang, S.-Y., Kim, J., & Poplawski, A. (2023). The potential benefits of companion robotic pets on the quality of life among community-dwelling older women. *Innovation in Aging, 7*(S1), 895-896. doi: 10.1093/geroni/igad104.2881
5. Landrum, J. (2025, March 30). *The rise of robot pets: Could AI replace living companions? 20 pros and cons*. Exploring Animals. https://exploringanimals.com/the-rise-of-robot-pets-could-ai-replace-living-companions/
6. Pico-Valencia, P., & Holgado-Terriza, J. A. (2025). The internet of things empowering the internet of pets – An outlook from the academic and scientific experience. *Applied Sciences, 15*(4), 1722. doi: 10.3390/app15041722
7. PsychCentral. (2022, July 26.) Robotic pets: As good for mental health as the real thing? PsychCentral. https://psychcentral.com/health/robotic-pets

8. Reference.com. (2015, August 4). *How do living and nonliving things interact in the environment?* https://www.reference.com/science-technology/living-nonliving-things-interact-environment-e6c4f0a19cda2b4d
9. Riddoch, K. A., Hawkins, R. D., & Cross, E. S. (2022). Exploring behaviours perceived as important for human-dog bonding and their translation to a robotic platform. *PLoS One, 17*(9), e0274353. doi: 10.1371/journal.pone.0274353
10. Wikipedia. (2024, May 16). *Human bonding*. https://en.wikipedia.org/wiki/Human_bonding
11. Wikipedia. (2025, January 19). *Neoteny in humans*. https://en.wikipedia.org/wiki/Neoteny_in_humans
12. Wikipedia. (2025, January 23). Neoteny. https://en.wikipedia.org/wiki/Neoteny

PURINA Institute
Advancing Science for Pet Health

GET TO KNOW THE PURINA INSTITUTE

Advancing Science for Pet Health

At the Purina Institute, we believe science is more powerful when it's shared. That's why we're on a mission to unlock the power of nutrition to help pets live better, longer lives. A global professional organization, the Purina Institute shares Purina's leading-edge research, as well as evidence-based information from the wider scientific community, in an accessible, actionable way so veterinary professionals are empowered to put nutrition at the forefront of pet health discussions to further improve and extend the healthy lives of pets through nutrition.

For more information and a wealth of pet nutrition resources,
visit PurinaInstitute.com and sign up for scientific communications.
By signing up, you'll receive updates on discoveries in nutritional science, free resources to support you in your nutrition conversations with clients, invitations to events, newsletters, and much more from the Purina Institute.

PurinaInstitute.com/Sign-Up

Learn more at
PurinaInstitute.com