Andreas R Pfenning

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Assistant Professor, January 2016-present
Computational Biology Department, School of Computer Science
Courtesy Appointment in Department of Biological Sciences, Mellon College of Science
Center for the Neural Basis of Cognition Member
Carnegie Mellon University

Google Scholar (link)   Pubmed (link)

Summary:

Many aspects of the brain, like the predisposition to neurological disorders and the ability to produce complex behavior, are encoded in our genome. The goal of my group is to build a set of computational and genomic tools to study how genetics and epigenetics influences neurons, neural circuits, disease, and behavior. We apply those techniques to study how regulatory regions have evolved to establish the neural circuits for speech and language. Within the human population, we study the genetic and epigenetic basis of aging, Alzheimer's disease, addiction, and psychiatric disorders.

Education:

MIT, Cambridge, MA
Postdoctoral Associate, 2012-2015
Advisor: Dr. Manolis Kellis, MIT/EECS and Broad Institute
Co-Advisor: Dr. Jesse M Gray, Harvard Medical School, Department of Genetics

Duke University, Durham, NC (GPA: 3.8)
Ph.D. Computational Biology and Bioinformatics, 2006-2012
Advisor: Erich D Jarvis, Howard Hughes Medical Institute, Department of Neurobiology
Co-Advisor: Alexander J Hartemink, Department of Computer Science

Carnegie Mellon University, Pittsburgh, PA (GPA: 3.8)
B.S. Computer Science, 2002-2006
College Honors Thesis and University Honors
Advisors: Dr. Alison L Barth, Dr. Russell Schwartz, Department of Biological Sciences

Research Areas:

➢ Genetic basis of neurological disorders and substance abuse
➢ Genetics and epigenetics of aging
➢ Evolution of complex behaviors and neural circuits, with a focus on speech/vocal learning in vertebrates
➢ Epigenomics of neural cell types

Journal Publications:

1. Wirthlin M, Chang EF, Knörnschild M, Krubitzer LA, Mello CV, Miller CT, **Pfenning AR**, Vernes SC, Tchernichovski, Yartsev MM. A Modular Approach to Vocal Learning: Disentangling the Diversity of a Complex Behavioral Trait. (2019) Neuron (link)

2. Glorioso C*, **Pfenning AR***, Bennett DA, DeJager PL, Sibille E, Kellis M, Guarente L. Glorioso C*, Pfenning AR*, Bennett DA, DeJager PL, Sibille E, Kellis M, Guarente L. Brain aging and APOE4 are independent additive predictors of neurological function and Alzheimer's disease. (2019) Life Sci Alliance (link)

3. Klein HU, McCabe C, Gjoneska E, Sullivan SE, Kaskow BJ, Tang A, Smith RV, Xu J, **Pfenning AR**, Bernstein BE, Meissner A, Schneider JA, Mostafavi S, Tsai LH, Young-Pearse TL, Bennett DA, De Jager PL. Epigenome-wide study uncovers large-scale changes in histone acetylation driven by tau pathology in aging and Alzheimer's human brains. (2019) Nature Neuroscience. (link)

4. Rossello RA, **Pfenning AR**, Howard JT, Hochgeschwender U. Characterization and genetic manipulation of primed stem cells into a functional naïve state with ESRRB. (2016) World J Stem Cells. (link)

5. Nguyen TA*, Jones RD*, Snavely A, **Pfenning AR**, Kirchner R, Hemberg M, Gray JM. High-throughput functional comparison of promoter and enhancer activities. (2016) Genome Research. (link)

6. Lyons M, Chen L-F, Deng J, Finn C, **Pfenning AR**; Sabhlok A, Wilson K, West AE. The transcription factor CaRF limits NMDAR-dependent transcription in the developing brain. (2016) J Neurochem. (link)

7. Madabhushi R, Gao F, **Pfenning AR**, Pan L, Yamakawa S, Seo J, Rueda R, Phan T, Pao P-C, Stott RT, Gjoneska E, Nott A, Cho S, Kellis M, Tsai L-H. Programmed DNA double strand breaks govern the expression of early response genes in neurons. (2015) Cell. (link)

8. Gjoneska E*, **Pfenning AR***, Mathys M, Quon G, Kundaje A, Tsai L-H, Kellis M. Conserved epigenomic signals in mice and human reveal immune basis of Alzheimer's disease. (2015) Nature. (link)

9. Kundaje A, Meuleman W, Ernst J, et al. (Author #21/93, equal contribution with first author in integrative analysis) Integrative analysis of 111 reference human epigenomes. (2015) Nature. (link)

10. **Pfenning, AR**, Hara E, Whitney O, Rivas M, Roulhac P, Ganapathy G, Hartemink AJ, Jarvis ED. Convergent transcriptional specializations in the brains of humans and song learning birds. (2014) Science. (link)

11. Whitney O*, **Pfenning AR***, Howard JT, Blatti CA, Lie F, Ward JM, Wang R, Kellis M, Mukherjee S, Sinha S, Hartemink AJ, West AE, Jarvis ED. Core and region enriched networks of behaviorally regulated genes and the singing genome. (2014) Science. (link)

12. Zhang G, Li C, Li Q, Li B, et al. (Author #51/105). Comparative Genomics Reveal Insights into Avian Genome Evolution and Adaptation. (2014) Science. (link)

13. Chen CC, Winkler CM, **Pfenning AR**, Jarvis ED. Molecular profiling of the developing avian telencephalon: regional timing and brain subdivision continuities. (2013) J Comp Neurol. PMID: 23818174 (link)

14. Jarvis ED, Yu J, Rivas MV, Horita H, Feenders G, Whitney O, Jarvis SC, Jarvis ER, Kubikova L, Puck AE, Siang-Bakshi C, Martin S, McElroy M, Hara E, Howard J, **Pfenning A**, Mouritsen H, Chen CC, Wada K. Global view of the functional molecular organization of the avian cerebrum: mirror images and functional columns. (2013) J Comp Neurol. PMID: 23818122 (link)

15. Liedtke W, McKinley MJ, Walker LL*, Zhang H*, **Pfenning AR***, Drago J, Hochendoner SJ, Hilton DL, Lawrence AJ, Denton DA. Relation of addiction genes to hypothalamic gene changes subserving genesis and gratification of a classic instinct, sodium appetite. (2011) Proc Natl Acad Sci. PMID: 21746918 (link)

16. **Pfenning AR**, Kim TK, Spotts JM, Hemberg M, Su D, West AE. Genome-wide identification of calcium-response factor (CaRF) binding sites predicts a role in regulation of neuronal signaling pathways. (2010) <u>PLoS One</u>. PMID: 20523734 (link)

17. **Pfenning AR**. Reverse Engineering Biological Networks: Opportunities and Challenges in Computational Methods for Pathway Inference. *Review.* (2010) <u>The Quarterly Review of Biology</u>.

18. Warren WC, Clayton DF, et al. (Author #36/80). The genome of a songbird. (2010) <u>Nature</u>. PMID: 20360741 (link)

19. **Pfenning AR**, Schwartz R, Barth AL. A comparative genomics approach to identifying the plasticity transcriptome. (2007) <u>BMC Neurosci</u>. PMID: 17355637 (link)

Manuscripts under review:

1. Ramamurthy R, Welch G, Cheng J, Yuan Y, Gunsalus L, Bennett DA, Tsai L-H, **Pfenning AR**. Cell type-specific histone acetylation profiling of Alzheimer's Disease subjects and integration with genetics. (2020) (preprint link)

2. Damas J, Hughes GM, Keough KC, Painter CA, Persky NS, Corbo M, Hiller M, Koepfli K-P, **Pfenning AR**, Zhao H, Genereux DP, Swofford R, Pollard KS, Ryder OA, Nweeia MT, Lindblad-Toh K, Teeling EC, Karlsson EK, Lewin HA. Epigenome-wide study uncovers large-scale changes in histone acetylation driven by tau pathology in aging and Alzheimer's human brains. (2020) (preprint link)

3. He J*, Kleyman M*, Alikaya A, Ozturk BE, Rothenhoefer KM, Wirthlin M, Fish K, Byrne LCT, **Pfenning AR**, Stauffer WR. Medium Spiny Neuron Diversity in the Primate Nucleus Accumbens. (2020)

Manuscripts in revision:

1. Zhang X*, Kaplow IM*, Wirthlin M, Park TY, **Pfenning AR**. HALPER facilitates the identification of regulatory element orthologs across species. (2020) (github link).

2. Yang J-H, Griffin PT, Vera DL, Apostolides JK, Hayano M, Meer MV, Salfati EL, Su Q, Munding EM, Blanchette M, Bhakta M, Dou Z, Xu C, Pippin JW, Creswell ML, O'Connell BL, Green RE, Garcia BA, Berger SL, Oberdoerffer P, Shankland SJ, Gladyshev VN, Rajman LA, **Pfenning AR**, Sinclair DA. Erosion of the Epigenetic Landscape and Loss of Cellular Identity as a Cause of Aging in Mammals (2020) (preprint link)

3. Genereux DP, Serres A, Armstrong J, Johnson J, Marinescu VD, Murén E, Juan D, Bejerano G, Casewell NR, Chemnick LG, Damas J, Di Palma F, Diekhans M, Fiddes IT, Garber M, Gladyshev VN, Goodman L, Haerty W, Houck ML, Hubley R, Kivioja T, Koepfli K-P, Kuderna LFK, Lander ES, Meadows JRS, Murphy WJ, Nash W, Noh HJ, Nweeia M, Pfenning AR, Pollard KS, Ray D, Shapiro B, Smit A, Springer M, Steiner CC, Swofford R, Taipale J, Teeling EC, Turner-Maier J, Alfoldi J, Birren B, Ryder OA, Lewin H, Paten B, Marques-Bonet T, Lindblad-Toh K, Karlsson EK. A comparative genomics multitool for scientific discovery and conservation. (2020)

   ***** Star indicates equal contribution*

Funding (Current):

American Federation for Aging Research   8/15/2018-8/15/2020 $50,000
Junior Faculty Grant – Cell type-specific epigenetic decay underlying brain aging

NIH – National Institute of Drug Abuse   8/15/2018-8/15/2023 $1,500,000
DP1 – Interpreting the regulatory mechanisms underlying the predisposition to substance use disorders

Sloan Research Fellowship   9/15/2018-9/15/2020 $65,000
Computational & Evolutionary Molecular Biology – Evolution of Regulatory Element Function

NIH - RFA-MH-19-135 (PI Stauffer)   07/01/2019-06/30/2024 $322,607
A massive library of AAVs to target transcriptionally-defined primate cell types

Center for Machine Learning and Health   09/01/2019-09/01/2020 $185,000
Developing a predictive epigenetic biomarker of Alzheimer's disease.

NIH – NIDA CNSA Pilot (*funds pending*)   06/01/2020-05/31/2021 $33,050
Applying single nucleus genomics to dissect conserved cell type-specific genetic mechanisms underlying addiction

Funding (History):

The Okawa Foundation   12/01/2016 $10,000
Interpreting Alzheimer's-associated genetic variation using genomic analysis

Whitehall Foundation   8/15/2018-8/15/2019 $75,000
Gene regulatory mechanisms underlying motor learning

Oral Presentations:

1. **Pfenning AR** (*March 2020*) Invited Speaker, Cell Type-Specific Transcriptome and Epigenome Abnormalities in Neurodegeneration. Neuroepigenetics and Neuroepitranscriptomics Conference. Nassau, Bahamas.

2. **Pfenning AR** (*January 2020*) Speaker, Addiction-associated genetic variants implicate cell type- and region-specific cis-regulatory elements in addiction neurobiology. National Institute of Health, Bethesda, Maryland.

3. **Pfenning AR** (*October 2020*) Invited Speaker. Epigenetic Mechanisms Underlying the Evolution of Learned Vocal Behavior. Broad Institute, Cambridge, MA.

4. **Pfenning AR** (*April 2019*). A data-driven approach to understanding Alzheimer's disease predisposition and progression. Annual Begeman Lecture, Northern Iowa University, Cedar Falls, Iowa.

5. **Pfenning AR** (*March 2019*) Speaker. Keystone Epigenetics and Disease. Epigenomic profiling of major human brain cell types reveals sex specific differences in hippocampal oligodendrocyte gene regulation in Alzheimer's Disease. Banff, Canada.

6. **Pfenning AR** (*November 2018*) Speaker, Panel Discussant. Tobacco Research Retreat. From genetics to neural circuits: The cell types underlying tobacco use. Pittsburgh, PA.

7. **Pfenning AR** (*November 2018*) Speaker, Panel Discussant. Society for Neuroscience Meeting Professional Development Seminar. Cultivating Leadership in Multidisciplinary Research: Bridging Gaps Across Campuses, Countries, and Continents. San Diego, CA.

8. **Pfenning AR** (*October 2018*) Invited Speaker, Fox Chapel High School Bioinformatics Research Symposium. A data-driven approach to Alzheimer's disease. Fox Chapel, PA.

9. **Pfenning AR** (*August 2018*) Invited Speaker, Max Planck Institute for Psycholinguistics. A comparative genomics approach to understanding the genetic basis of vocal learning behavior. Nijmegen, Netherlands.

10. **Pfenning AR** (*April 2018*) Invited Speaker, Pittsburgh Chromatin Club Meeting. DNA damage drives aging and epigenetic decay of cell type identity. Pittsburgh, PA.

11. **Pfenning AR** (*February 2018*) Invited Speaker, Epigenetic dissection of regulatory elements underlying the evolution of learned vocal behavior. Neuroepigenetics and Neuroepitranscriptomics Conference. Cancun, Mexico.

12. **Pfenning AR** (*January 2018*) Speaker, Cell Type and Brain Region-Specific Impact of Nicotine Use-Associated Genetic Variation. National Institute of Health, Bethesda, Maryland.

13. **<u>Pfenning AR</u>** (*October 2017*) Panel Discussant, Modeling the Opioid Epidemic Workshop. University of Pittsburgh. Pittsburgh, PA.

14. Wirthlin M, **<u>Pfenning AR</u>** (*July 2017*) Epigenetic Mechanisms Underlying the Evolution of Learned Vocal Behavior. Society for Molecular Biology and Evolution Meeting, Austin TX.

15. **<u>Pfenning AR</u>** (*May 2017*) Cell type-specific epigenomic changes during aging and neurodegeneration. Department of Genetics Seminar. Stanford University, Stanford CA.

16. **<u>Pfenning AR</u>** (*April 2017*) A data-driven approach to understanding the genetic basis of Alzheimer's disease. Medicine in silico: Artificial Intelligence and Diagnostics, Stanford University, Stanford CA.

17. **<u>Pfenning AR</u>** (April 2017) Translating genetic findings into new therapies for Alzheimer's disease. Project Olympus Show and Tell, Carnegie Mellon University, Pittsburgh PA.

18. **<u>Pfenning AR</u>** (February 2017) Towards identifying convergent evolution in the genome for vocal learning. Biology Seminar, University of Pittsburgh, Pittsburgh PA.

19. **<u>Pfenning AR</u>** (February 2017) Genomic insights into the genetic basis of aging. Molecular Medicine Research Seminar, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, Pittsburgh PA.

20. **<u>Pfenning AR</u>** (March 2016) Pfenning AR (February 2016) Genomic insights into the immune basis of Alzheimer's disease and aging. Brain Lunch Seminar, Massachusetts Institute of Technology, Cambridge, MA.

21. **<u>Pfenning AR</u>** (February 2016) Genomic insights into the immune basis of Alzheimer's disease and aging. Computational Biology and Bioinformatics Invited Seminar, Duke University, Durham NC.

22. **<u>Pfenning AR,</u>** Gjoneska E, Kundaje A, Quon G, Giallourakis C, Kellis M, Tsai L-H. (*December 2015*) An Investigation into the impact of Alzheimer's disease on the enhancer landscape in mice and humans. Syros Pharmaceuticals, Cambridge, MA.

23. **<u>Pfenning AR</u>**, Glorioso C, Wu S, Sibille E, Bennet DA, Chibnik L, De Jager P, Kellis M, Guarente L. (December 2015) Towards the genetic basis of brain aging. GTEx Investigator Meeting, Bethesda, MD.

Awards and Activities:

2018	Sloan Research Fellow
2018	AFAR Junior Investigator
2017-present	Member, Vertebrate Genome Project Consortium
2016	Okawa Foundation Research Grant in Bioinformatics
2014	Kavli Foundation Blog – Biggest Science Stories of 2014: Neuroscience Human Speech Similar to Birdsong
2013	Best Postdoc Poster Presentation, Harvard Med. Genetics Retreat

2013	ISMB/ECCB Conference Program Committee
2012-present	Member, AAAS
2012-2015	Member, American Society for Human Genetics
2006-present	Member, Phi Beta Kappa
2006-present	Member, Society for Neuroscience
2010	Best Poster Presentation, Duke Computational Biology
2007-2009	Computational Biology Student Committee
2006	Richard Schoenwald Phi Beta Kappa Research Award
2005	Carnegie Mellon Small Undergraduate Research Grant

Selected Press Coverage of Research:

Genetics of Alzheimer's disease (2017)
  ➢ WESA (NPR Radio) – "Tech Highlights"
  ➢ KDKA (CBS Television) – Discussing Alzheimer's genes and importance of research

Conserved epigenomic signals in mice and human reveal immune basis of Alzheimer's disease and Integrative analysis of 111 reference human epigenomes
  ➢ MIT News – "Study of epigenomic modifications reveals immune basis of Alzheimer's disease"
  ➢ Boston Globe – "New research sheds light on cancer, Alzheimer's origins"
  ➢ The Economist – "Epic genomics"
  ➢ Science News – "Massive project maps DNA tags that define each cell's identity"
  ➢ PBS Newhour – "A detailed new map of our genome in action"
  ➢ New York Times – "Project Sheds Light on What Drives Genes"
  ➢ Genomeweb – "Roadmap Epigenomics Consortium Members Publish Study Collection"

Convergent transcriptional specializations in the brains of humans and song learning birds
  ➢ ABC News/AP – "New Family Tree for Birds Spurs Ideas on Evolution"
  ➢ New Scientist – "Humans and birds share the same singing genes"
  ➢ NPR, All things considered – "Birds Of A Feather Aren't Necessarily Related"
  ➢ Washington Post – "Birdsong and human speech turn out to be controlled by the same genes"
  ➢ Newsweek – "How Stuttering Songbirds Could Cure It in People"
  ➢ Science News – "Bird genomes give new perches to old friends"
  ➢ Nature News – "Flock of geneticists redraws bird family tree"
  ➢ MIT News – "Could birdsong help us solve stuttering?"

Relation of addiction genes to hypothalamic gene changes subserving genesis and gratification of a classic instinct, sodium appetite
  ➢ National Geographic – "Cocaine Addiction Uses Same Brain Paths as Salt Cravings"
  ➢ Sydney Morning Herald – "Addictive drugs hijack brain's fundamental pathways"
  ➢ Spiegel Online – "Salz, Drogen und der Streit um den Blutdruck"

The genome of a songbird
  ➢ BBC – "Blueprint of the songbird genome"
  ➢ New York Times – "From a Songbird, New Insights Into the Brain"

Mentoring:

Current
- 2 postdoctoral fellows
- 5 PhD students (3 CPCB, 1 Biological Sciences, 1 CPCB/MDPhD)
- 2 Masters students

- 5 current undergraduate research students at Carnegie Mellon

Previous
- 2 masters students
  - Sarah Hsu (Research Scientist at Broad Institute)
  - Meaghan Kennedy (PhD Student at UNC)
- 5 undergraduates
  - Sid Annaldasula (Fulbright fellowship, Max Planck Institute of Molecular Genetics)
  - Laura Gunsalus (PhD Student at UCSF)
  - Tae Yoon Park (PhD Student at Princeton)
  - Christine Xu (Research Assistant at Stanford University School of Medicine)
  - Yixin Yuan (Simons Fellows in Computational Neuroscience, Emory University School of Medicine)

Teaching:
- Professor, Introduction to Computational Biology (Spring 2018, Spring 2019; Spring 2020 CMU, 02-250,03-250)
- Professor, Genomics and Epigenetics of the Brain (Spring 2017, Fall 2018; CMU, 02-319,02-360,02-719,03-760)
- Professor, Cell and Systems Modeling (Fall 2016, CMU, 02-740)

Leadership/Outreach Activities:
- Advocacy
  - Meeting with congressional staff to advocate for increases to Alzheimer's disease research funding (November 2017)
    - Provided quantitative arguments for not taxing graduate student stipends.
- Conference Leadership
  - Session Chair, Comparative Genomics, Genome 10K Annual Conference, New York, NY. (September 2018)
  - Session co-chair, Biomedical Sciences, Artificial Intelligence and Data Re-use (NSF funded), Pittsburgh, PA. (May 2019).
- Computational Biology Undergraduate Curriculum Committee (current)
  - Active role in defining courses that will make up the major
  - Meeting with prospective majors
- Neuroscience Undergraduate Curriculum Committee (current)
  - Working to bridge computational neuroscience with computational biology
- Assisted in curriculum design for Systems Neuroscience Graduate Program
- CMU Neuroscience Institute Planning Committee
- Outreach:
  - Carnegie Mellon SCS Alumni Advisory Board Research Presentation
  - Neurohackathon dataset provider
  - Speaking at local high schools about the field of computational biology
  - Panel speaker on funding opportunities in neuroscience
  - Panel speaker on finding postdoctoral opportunities in biology
  - Scientific Advisor, Anya (movie, expected 2019)
  - Undergraduate research award committee (previous)
- Faculty Search Committee Experience
  - Systems Neuroscience Faculty Search (2019)
  - Pittsburgh Supercomputing Center Director Search Committee (2019)
- Computational Biology PhD admissions committee (2018)

Journal/Conference/Grant Reviews
- Reviewed paper(s) for the following journals
    - Nature Neuroscience – 1
    - Nature Genetics – 1
    - Molecular Ecology – 1
    - Great Lakes Bioinformatics – 1
    - Nature Medicine – 2
    - Cell – 1
    - F1000 – 1
    - Bioinformatics – 1