

Trans-generational epigenetic inheritance in living and digital hyenas

Background: Epigenetics is the study of functional, often heritable, changes in gene activity not caused by changes in the nucleotide sequence of DNA molecules. Although phenotypes are certainly dependent upon the presence of particular genes, the selective silencing or activation of genes is equally critical (Champagne 2013). Epigenetics affect evolution when epigenetic changes are heritable. Two important ways in which epigenetic inheritance can differ from traditional genetic inheritance, with important consequences for evolution, are that 1) rates of epimutation can be much faster than rates of mutation (Rando & Verstrepen 2007), and 2) epimutations are more easily reversible (Lancaster & Masel 2009). Recent work in epigenetics has forced us to expand "the modern evolutionary synthesis" to include heritable changes in gene expression patterns that are induced during development by environmental stimuli, and that help shape the phenotypes on which natural selection operates (Jablonka & Raz 2009; Muller 2007; Bossdorf et al. 2008; Wray et al. 2014). During the past decade, epigenetically-mediated developmental plasticity has come to represent a critical aspect of evolutionary developmental biology, and computer scientists have also recently started to appreciate the implications of epigenetics for machine learning and robotics (e.g., Tanev & Tuta 2004; Turner et al. 2010). In both biological and computational systems, epigenetically-mediated developmental plasticity can bias evolution and enhance evolvability (Richards et al. 2010).

In fluctuating environments, epigenetic modification can theoretically permit young mammals to enhance their fitness by adjusting their phenotypes to match the environment they will experience at independence (Dantzer et al. 2013). ***Here we propose to combine field study of wild hyenas with evolution in silico of digital hyenas to test a hypothesis suggesting that epigenetic mechanisms match offspring phenotypes to current environmental conditions, and thereby permit crossing of fitness valleys imposed by fluctuating environments.*** It is now well-established that early life experiences can produce persistent and heritable epigenetic effects on mammalian brains and behavior (Hunter & McEwen 2013). The brain mediates perception of, and responses to, stress, and laboratory rodent models show that epigenetic mechanisms shape stress-related physiology and behavior across the lifespan and beyond to succeeding generations. DNA methylation, the covalent addition of a methyl group to CpG dinucleotides, is the most stable and best-characterized epigenetic mechanism. Not only does DNA methylation regulate expression of specific genes, but genome-wide methyl-group content ("global DNA methylation") confers genomic stability (Allis et al. 2007). DNA methylation patterns are highly modifiable during early ontogeny, suggesting that they might adjust offspring phenotypes to current social and ecological conditions. In laboratory rodents exposure to adverse social environments shortly after birth alters methylation of the glucocorticoid receptor (**GR**) gene and leads to its modified expression in stress-related physiology and behavior (Francis et al. 1999; Weaver et al. 2004); interestingly these effects persist over multiple generations (Daxinger & Whitelaw 2012; Guerrero-Bosagna & Skinner 2012). Similarly, early exposure to synthetic stress hormones causes changes in global DNA methylation in lab rodents that persist for at least three generations (Crudo et al. 2012). However, it is currently unknown how long effects of trans-generational epigenetic inheritance last, or how they function, in nature. Here we will pair computational modeling efforts with molecular data from living hyenas to ask whether global and gene-specific methylation patterns vary with specific types of stressful environmental fluctuations, over how many generations both types of methylation patterns persist in nature, and under what conditions epigenetic mechanisms enhance fitness.

We will use wild hyenas to test a hypothesis suggesting that adverse environmental conditions shortly after birth alter GR methylation in the wild as they do in lab rodents, and determine the extent to which gene-specific and global patterns of DNA methylation persist when measured in up to 8 consecutive generations of hyenas. Early adversity in hyenas might involve low social rank, poor maternal care, high lion density, drought, or some combination of these variables. We will use computer simulations to mimic epigenetic gene regulation and test the hypothesis that epigenetic effects can potentially facilitate crossing of fitness valleys by manipulating the selective conditions shaping fitness landscapes in digital systems with fast generation times. Specifically we can ask whether epigenetic modifications match hyena phenotypes to current environmental conditions, and how many generations a particular modification would theoretically need to persist to permit crossing of various sorts of fitness valleys.

Methods with living hyenas: Using archived samples and behavioral data from members of six hyena clans monitored in our long-term field study, we will bring together measures of fitness, quality of maternal care, global DNA methylation, GR methylation, short-lived stressors (e.g., drought), longer-term stressors (e.g. low social rank or high lion density), stress-related behavior, and stress hormone concentrations. Our wild hyenas are routinely immobilized and their DNA extracted. Maternal care will be assessed with data on mothers' den attendance, nursing, food provisioning, and protective interventions (Smale et al. 1993). For each clan, we have a full pedigree that provides accurate relatedness data for 8 generations of hyenas. We will measure global DNA methylation using the Luminometric assay (Karimi et al. 2006) following a standard protocol (Sant et al. 2012). We will determine promoter region methylation of the GR gene; we have recently sequenced the GR gene in hyenas, and will determine GR methylation using a highly reproducible pyrosequencing-based technology and PyroQ-CpG software (Qiagen).

Methods with digital hyenas: Here we will use a computational model of “digital hyenas” to inquire how epigenetic mechanisms might enhance the ability to cope with fluctuating environments better than would ordinary genetic modification. For epigenetic effects to enhance fitness, environmental fluctuations should theoretically be sufficiently short-lived to favor leaving underlying gene sequences intact, and only modifying the genome temporarily, perhaps because environmental conditions are likely to return within one or a few generations to some earlier optima. The computational model will allow us to test the hypothesis that methylation permits rapid adaptation that confers a fitness advantage under such conditions. Fluctuations will be generated to model, for example, a drought that lasts variable numbers of generations, forcing the hyenas to alter their foraging behavior because of diminished prey. Another fluctuation might be sudden changes in the populations of other predators such as lions, forcing the hyenas to avoid behaviors that attract lions. Such changes create fitness valleys that change too quickly for genetic evolution to track but that should nevertheless favor individuals predisposed to behave in particular ways. Miikkulainen will simulate digital hyenas based on technology developed in our earlier collaborations: a simulated environment will be created with prey and predators with various capabilities (speed, abundance, value); artificial neural networks (ANNs) will control the hyenas' behavior in this environment based on sensory input. Hintze will run similar models using Markov Gate Networks to inquire whether epigenetic modifications permit rapid adaptation to fluctuating social conditions. The ANNs will be evolved through genetic algorithms such as NEAT to hunt prey and avoid predators with different strategies. However, in the proposed work a new mechanism will be added to the neuroevolution method: the epigenetic effect of methylation affecting gene expression. The mechanism builds on two previous ideas in evolving neural networks for changing environments: selecting parts of the network to perform different behaviors at different times (Schrum 2014), and augmenting evolution with fast adaptation (Valsalam et al. 2007). In the NEAT genetic encoding, each gene (representing a node in the neural network) will carry a methylation value that represents the probability that that gene will not be expressed; this value decays over time. When a population faces a fitness valley (implemented as a change in prey or predator populations), methylation will be increased in each gene proportional to how active the corresponding node was in the behavior. As a result, the individual will favor alternative behaviors. These changes are heritable, and as shown by Valsalam et al (2007) and Schrum (2014), networks will evolve to utilize the fast adaptation and the distribution of behavior to perform well. The results of these experiments will be compared to digital evolution under identical environmental conditions, but in which we do not allow for epigenetic modifications, to test the hypothesis that epigenetic mechanisms match offspring phenotypes to current environmental conditions, and thereby permit crossing of fitness valleys imposed by fluctuating environments. The end result will be a computational theory of how the observed epigenetic effects might function in living organisms.

Plan for obtaining extramural funding: Here we will target two panels for extramural support once we have adequate pilot data: 1) the Animal Behavior panel in IOS at NSF and 2) funding opportunity PAR-13-374 at NIH (“Modeling Social Behavior”).

Intellectual Merit: This work will elucidate how early life experiences modulate gene expression and adult stress physiology in gregarious mammals, reveal whether and to what extent these epigenomic changes persist across generations, and how they affect fitness under specific social and ecological conditions in the natural habitat. To understand the full significance of epigenetic processes, it is imperative to study them in an ecological context (Bossdorf et al. 2008), but this has never been done before. Our computational model will allow us to test hypotheses suggesting how long epigenetic effects might theoretically endure, and under which types of environmental conditions animals might better enhance their fitness by epigenetic than genetic change. This work will have important implications both for understanding phenotypic variation in nature and for enhancing robustness and plasticity of machine learning in noisy environments (Reisinger & Miikkulainen 2007).

Broader impacts: Epigenetic processes are known to influence many aspects of human health and development, (Whitelaw & Whitelaw 2008). However to date these processes have only been examined in lab settings where effects of socioecological variables cannot be examined; thus our new model will add considerable realism to the study of epigenetic phenomena known to affect mammals with complex social lives and variable environments. In contrast to the work proposed here, most existing computational models of genetic regulatory networks are extremely complex, depend on the validity of many simplifying assumptions, and fail to include modifiability of gene expression as a result of experience during ontogenetic development (Bongard & Pfeifer 2003). Thus we believe the work proposed here should lead to significant improvements in the linkage between biological reality and computational models of epigenetic effects. We plan to develop a new graduate seminar at MSU on epigenetic effects on behavior. Finally, three graduate students (Elliot Meyerson at UT, Zach Laubach and Connie Rojas at MSU) and one undergrad (at MSU) will be trained on this project. Connie Rojas is a new female Hispanic BEACON graduate student.

References

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- Valsalam, V.K., Bednar J.A. & Miikkulainen, R. (2007) Developing Complex Systems Using Evolved Pattern Generators. *IEEE Transactions on Evolutionary Computation* 11: 181–198.
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Professional preparation

Smith College, Northampton, MA, Psychology & Biology, A.B. 1973
University of California, Berkeley, CA, Psychobiology, Ph.D. 1983
University of California, Santa Cruz, CA, N.R.S.A. Postdoc, Endocrinology, 1983-1986

Appointments

2009-present: Director, interdisciplinary program in Ecology, Evolutionary Biology & Behavior, Michigan State University
1999-present: Professor, Department of Zoology, Michigan State University
1992-1999: Assistant and Associate Professor, Department of Zoology, Michigan State University
1987-1991: Research Associate, Department of Ornithology and Mammalogy, California Academy of Sciences, San Francisco, CA.

Honors

Named AAAS Fellow, 2013
Recipient of the Smith College Medal, 2013
Named University Distinguished Professor, Michigan State University, 2009.
College of Natural Science Distinguished Faculty Award, Michigan State University, 2007.
University Distinguished Faculty Award, Michigan State University, 2006.
Recipient, C. Hart Merriam Award from the American Society of Mammalogists, 2005
Named Fellow of the Animal Behavior Society, 2001
Recipient, College of Natural Science Outstanding Academic Advisor Award, 2001
Recipient, Teacher-Scholar Award, Michigan State University, 1998.

Most relevant publications (total=127)

1. Van Meter, P. E., French, J. A., Dloniak, S. M., & **Holekamp, K. E.** (2009) Fecal glucocorticoids reflect socio-ecological and anthropogenic stressors in the lives of wild spotted hyena. Hormones and Behavior. 55: 329- 337
2. Dloniak, S.M., French, J. A. & **Holekamp, K. E.** (2006) Rank-related maternal effects of androgens on behaviour in wild spotted hyenas. Nature. 440: 1190-1193.
3. **Holekamp, K.E.**, Smith, J. E., Strelhoff, C. C., Van Horn, R.C. & Watts, H. E. (2012) Society, demography and genetic structure in the spotted hyena. Molecular Ecology. 21, 613–632.
4. Rawal, A., Rajagopalan, P., **Holekamp, K. E.** & Miikkulainen, R. (2012) Evolution of a Communication Code in Cooperative Tasks. In Proceedings of Thirteenth International Conference on the Synthesis and Simulation of Living Systems (Alife'13, East Lansing, MI).
5. Rajagopalan, P., Rawal, A., Miikkulainen, R., Wiseman, M. A. & **Holekamp, K. E.** (2011) The role of reward structure, coordination mechanism and net return in the evolution of

cooperation. 2011 IEEE Conference on Computational Intelligence and Games. Pp. 258-265.

Other significant publications

1. Lewin, N., Treidel, L. A., **Holekamp, K. E.**, Place N.J., & Haussmann, M.F. (2015) Socioecological variables predict telomere length in wild spotted hyenas. Biology Letters. In press.
2. Rajagopalan, P., Rawal, A., **Holekamp, K.E.**, & Miikkulainen, R. (2014) General intelligence through prolonged evolution of densely connected neural networks. Proceedings of the 2014 Genetic and Evolutionary Computation Conference (GECCO-2014), Vancouver, Canada.
3. Rawal, A., Rajagopalan, P., Miikkulainen, R., & Holekamp, K. E. (2012). Evolution of a Communication Code in Cooperative Tasks. Artificial Life 13: 243-250.
4. Gersick, A.S., Cheney, D.L., Schneider, J. M., Seyfarth, R. M. & **Holekamp, K. E.** (2015) Long-distance communication facilitates cooperation among spotted hyenas (*Crocuta crocuta*). Animal Behaviour. In press
5. **Holekamp, K. E.** & Dloniak, S. M. (2010) Intra-specific variation in the behavioral ecology of a tropical carnivore, the spotted hyena. Advances in the Study of Behavior. 42: 189-229.

Synergistic activities:

- 1) Annually teach a graduate class (ZOL801) on Ethics, Grantsmanship & Professional Development at MSU (2005-present).
- 2) Service as a reviewer: Member, Editorial review board for *Nature Communications* (2010-present). Ad hoc reviewer for NSF, and reviewer for *Nature*, *PNAS*, *Journal of Mammalogy*, *Animal Behaviour*, *Behavioral Ecology*, *Acta Theriologica*, *Journal of Zoology London*, *Hormones and Behavior*, *Behavioral Ecology and Sociobiology*, *Proceedings of the Royal Society*, *African Journal of Ecology*, and *Physiological Zoology*.
- 3) Advisory service: Member, Scientific Advisory Committee for the MSU Museum, 2004-present. Faculty advisor for *Kila Nafasi* Student Group (a charitable organization based at MSU dedicated to raising funds to educate Masai women; *Kila Nafasi* is Swahili for "Every Opportunity"), 2008-present. Advisor for Honors College undergraduates majoring in Zoology, MSU, 1997-present. Member Kenya Wildlife Service Committee on Carnivore Conservation, 2001-present.
- 4) Work with public media: Logistic assistance in Kenya and scientific advice to film crews from BBC, Animal Planet, Discovery Channel, Big 10 Channel, and various film crews from Europe and Asia. Contributions to *New York Times* "Scientists at work" blog, and the research blog we maintain for the Mara Hyena Project called "Notes from Kenya." Host reporters at our field site from print media outlets around the world.
- 5) Chair of the IUCN Hyaena Specialist Group (2008-present) & maintenance of an educational IUCN website about hyaenids at <http://www.hyaenidae.org/>.

BIOGRAPHICAL SKETCH

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Professional Preparation

Helsinki University of Technology	Applied Mathematics	MS 1986
University of California, Los Angeles	Computer Science	PhD 1990

Appointments

Professor, Department of Computer Sciences, The University of Texas at Austin, since 2002;
Associate Professor, 1996–2002; Assistant Professor, 1990–1996.
Faculty Member, the Institute for Neuroscience, The University of Texas at Austin, since 2000.

Five Most Relevant Publications

- Rawal, A., Boughman, J. and Miikkulainen, R. (2014). Evolution of Communication in Mate Selection. In *Proceedings of The Fourteenth International Conference on the Synthesis and Simulation of Living Systems* (Alife' 14, New York, NY).
- Rajagopalan, P., Holecamp, K. E., and Miikkulainen, R. (2014). The Evolution of General Intelligence. In *Proceedings of The Fourteenth International Conference on the Synthesis and Simulation of Living Systems* (Alife' 14, New York, NY).
- Valsalam, V., Hiller, J., MacCurdy, R., Lipson, H., and Miikkulainen, R. (2012). Constructing Controllers for Physical Multilegged Robots using the ENSO Neuroevolution Approach. *Evolutionary Intelligence* 5:45–56. <http://nn.cs.utexas.edu/?valsalam:evolint12>
- Kohl, N. and Miikkulainen, R. (2012). An Integrated Neuroevolutionary Approach to Reactive Control and High-level Strategy. *IEEE Transactions on Evolutionary Computation*, 16:472–488. <http://nn.cs.utexas.edu/?kohl:ieetec11>
- Valsalam, V. and Miikkulainen, R. (2011). Evolving Symmetry for Modular System Design. *IEEE Transactions on Evolutionary Computation*, 15:368–386. <http://nn.cs.utexas.edu/?valsalam:ieetec07>.

Five Other Publications

- Lehman, J. and Miikkulainen, R. (2013). Neuroevolution. *Scholarpedia* 8(6):30977.
- Lockett, A. and Miikkulainen, R. (2013). Evolutionary Annealing: Global Optimization in Borel Measure Spaces. *Journal of Global Optimization*. <http://nn.cs.utexas.edu/?lockett:jogo2013>
- Schrum, J. and Miikkulainen, R. (2012). Evolving Multimodal Networks for Multitask Games *IEEE Transactions on Computational Intelligence and AI in Games*, 4:94–111. <http://nn.cs.utexas.edu/?schrum:tciaig12>
- Gomez, F., Schmidhuber, J., and Miikkulainen, R. (2008) Accelerated Neural Evolution through Cooperatively Coevolved Synapses. *Journal of Machine Learning Research* 9:937–965. nn.cs.utexas.edu/?gomez:jmlr08.
- Stanley, K. and Miikkulainen, R. (2004). Competitive Coevolution through Evolutionary Complexification. *Journal of Artificial Intelligence Research* 21:63–100. nn.cs.utexas.edu/?stanley:jair04.

Synergistic Activities

Member of the Board of Governors, International Neural Network Society; Member of the IEEE Computational Intelligence Society Technical Committees for Computational Intelligence in Games; Member of the Distinguished Lecturer Program, IEEE Computational Intelligence Society.

Current or past associate/action editor, *IEEE Transactions on Autonomous Mental Development*, *IEEE Transactions on Computational Intelligence and AI in Games*, *Machine Learning*, *Neural Networks*, *Cognitive Systems Research*; Technical Program Co-Chair, *Congress on Evolutionary Computation* (CEC-2011), July 2011; Program Co-Chair, *2010 IEEE Conference on Computational Intelligence and Games* (CIG-10), August 2010; *Workshop on Self-Organizing Maps* (WSOM-09), October 2009; *IEEE Symposium on Computational Intelligence and Games* (CIG-08), December 2008.

Developer of 32 software packages for neuroevolution, natural language processing and computational neuroscience, nn.cs.utexas.edu/soft-list.php (with Matt Alden, Erkin Bahceci, Chris Ball, James A. Bednar, Bobby D. Bryant, Matt Buckland, Yoonsuck Choe, Julien Ciroux, Judah De Paula, Eliana Feasley, Aliza Gold, Faustino Gomez, Colin Green, Mattias Fagerlund, Derek James, Igor Karpov, Riitta Katila, Alan Lockett, Cynthia Matuszek, Marty Mayberry, Christian Mayr, David Moriarty, Alan Oursland, Jefferson Provost, Jacob Schrum, John Sheblak, Bryan Silverthorn, Joseph Sirosh, Yiu Fai Sit, Kenneth O. Stanley, Bram Stolk, Wesley Tansey, Philip Tucker, Vinod Valsalam, and Udo Vierucci).

Co-founder, *Digital Certainty, Inc.*, a startup focusing on evolutionary optimization in web commerce.

Winner, BotPrize Award (successfully passing a Turing test for game bots), at the *IEEE Conference on Computational Intelligence in Games* (CGI-12, Grenada, Spain), for the UT² program of Igor Karpov, Jacob Schrum, and Risto Miikkulainen.

Collaborators and Co-Editors (outside UT Austin)

Chris Adami (MSU), Michal Bida (Charles Univ. in Prague), Paolo Burelli (IT Univ. of Copenhagen), Alex Champandard (AIGameDev, Inc), Clare B. Congdon (Univ. of Southern Maine), Martin Ebner (Graz Univ. of Technology), Erik Goodman (MSU), Phil Hingston (Edith Cowan University), Ralph Hoffman (Yale), Kay Holekamp (MSU), Riitta Katila (Stanford), Graham Kendall (Nottingham), Ben Kerr (Univ. of Washington), Swathi Kiran (Boston University), Benjamin Kuipers (UMich), Daniele Loiacono (Politecnico di Milano), Pier Luca Lanzi (Politecnico di Milano), Rich Lenski (MSU), John Levine (Strathclyde), Hod Lipson (Cornell), Simon Lucas (Exeter) Charles Ofria (MSU), Rob Pennock (MSU), David Ress (Baylor), Clifford D. Saron (UC Davis), Tom Schaul (NYU), Sruthi Thatchenkery (Stanford), Tommy Thompson (Derby), Georgios Yannakakis (IT Univ. of Copenhagen).

Thesis Advisor and Postgraduate-Scholar Sponsor

Own PhD advisor: Michael G. Dyer (UCLA). Twentyeight PhD and nine postdoctoral advisees: Matt Alden (Univ. of Washington, Tacoma), Erkin Bahceci (Google, Inc.), James Bednar (Univ. of Edinburgh), Bobby D. Bryant (Univ. of Nevada, Reno), Harold Chaput (BioWare, Inc.), Yoonsuck Choe (Texas A&M University), Judah De Paula (Pioneer, Inc.), Igor Farkas (Comenius University, Slovakia), Faustino Gomez (IDSIA, Switzerland), Uli Grasemann (The Univ. of Texas at Austin), Elizabeth C. Kaczmarczyk, Nate Kohl (Google Inc.), Joel Lehman (The Univ. of Texas at Austin), Wee Kheng Leow (National Univ. of Singapore), Daniel Lessin (ITU Copenhagen), Alan Lockett (IDSIA, Switzerland), Paul McQuesten (Elite Analytics, Inc.), Marshall Mayberry (Univ. of California, Merced), David Moriarty (Apple, Inc.), Daniel Polani (Univ. of Hertfordshire, UK), Jefferson Provost (Apple, Inc.), Melissa Redford (Univ. of Oregon), Manish Saggarr (Stanford University), Jacob Schrum (Southwestern University), Yaron Silberman (Medigus Inc., Israel), Bryan Silverthorn (CTO, Angaza Design, Inc.), Joseph Sirosh (Amazon, Inc.), Yiu Fai Sit (Univ. of Texas at Austin), Kenneth O. Stanley (Univ. of Central Florida), Cem Tutum (Univ. of Texas at Austin), Tal Tversky (Apple, Inc), Vinod Valsalam (Twosigma, Inc) Austin Waters (Google, Inc).

Biographical Sketch: AREND HINTZE

A. Professional Preparation

Westfälische Wilhelms-Universität Münster, Germany	Biology	Diploma	1996
Technische Universität Braunschweig	Biology	Diploma	2001
Institute for Genetics, Braunschweig	Biology	Dr. rer.nat.	2006
Keck Graduate Institute	Computational Biology		2010

B. Academic and Professional Appointments

From 08/2015	Assistant Professor for Integrative Biology, Computer Science and Engineering, Michigan State University
06/2010 – 08/2015	Postdoctoral Research Associate, Michigan State University
04/2010 - 06/2011	Research Assistant Professor (on leave), Keck Graduate Institute
08/2006 - 04/2010	Postdoctoral Research Associate, Keck Graduate Institute
06/2001- 07/2006	Research Assistant, TU Braunschweig

C. Relevant Publications

- 1) Albantakis L., **Hintze A.**, Koch C., Adami C., Tononi G. (2014) *Evolution of Integrated Causal Structures in Animats Exposed to Environments of Increasing Complexity*. PLoS Comput Biol 10(12): e1003966. doi:10.1371/journal.pcbi.1003966
- 2) S. D. Chapman, D. B. Knoester, **A. Hintze**, and C. Adami. *Evolution of an artificial visual cortex for image recognition*. In: “Advances in Artificial Life (ECAL 2013)” (P. Liò, O. Miglino, G. Nicosia, S. Nolfi and M. Pavone, eds.) MIT Press (2013) pp. 1067-1074
- 3) **Hintze**, M. Miromeni, *Evolution of autonomous hierarchy formation and maintenance*, ALIFE 14: The Fourteenth Conference on the Synthesis and Simulation of Living Systems, MIT Press 2014, pp. 366-367
- 4) R. Olson, **A. Hintze**, F. Dyer, D. B. Knoester, C. Adami, *Predator Confusion is Sufficient to Evolve Swarming*, (Journal of the Royal Society Interface 10: 20130305 (2013))
- 5) **Hintze**, L. Marstaller, and C. Adami, *The Evolution of Representation in Simple Cognitive Networks*. *Neural Computation* 25 (2013) 2079-2105
- 6) Edlund, N. Chaumont, **A. Hintze**, C. Koch, G. Tononi, and C. Adami. *Integrated Information Increases with Fitness in the Evolution of Animats*. PLoS Comp. Biol. 7 (2011) e1002236.
- 7) Adami, J.Qian, M. Rupp, and **A. Hintze**. *Information content of colored motifs in complex networks*. *Artificial Life* 17 (2011) 375-390.
- 8) Qian, **A. Hintze**, and C. Adami. *Colored Motifs Reveal Computational Building Blocks in the C. elegans Brain*. PLoS ONE 6 (2011) e17013.
- 9) Marstaller, C. Adami, and **A. Hintze**. *Measuring Representation*. In: W. Christensen, E.

Biographical Sketch: AREND HINTZE

Schier, & J. Sutton (Eds.), ASCS09: Proceedings of the 9th Conference of the Australasian Society for Cognitive Science (pp. 232-237). Sydney, Australia: Macquarie Centre for Cognitive Science (2010).

- 10) Adami, N. Chaumont, J. Edlund, **A. Hintze**, *Topological properties of evolved robot brains*, *ALIFE XI conference*, Southampton (UK), 2008

D. Synergistic Activities

Referee for peer review journals:

PLoS Computational Biology, Proc. Natl. Acad. Sci. USA, Physical Review Letters, Physical Review E, Proc. Roy. Soc. Interface,

Program Committee of the Artificial Life conference XII, XIII

Published software applications for scientific computation:

C. elegans data analysis package, Windows application, 2006

Artificial Cell Model, C++ code, 2008

Antimodularity Toolkit, Matlab and C++ library collection, 2009

PHI computation toolkit, C++ library, 2009

EOS- Swarm Evolution Platform, C++ and Processing 2012

EvoSphere – Evolutionary framework to study coevolution of behavior and morphology in complex 3D physics environments (in preparation)

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