Talk 205 Neural Flow Networks in Songbirds (NIDCD R01-DC 007996 FY 05) Alexander J. Hartemink Duke University, Department of Computer Science

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Determining how information flows within neural pathways is a fundamental requirement for understanding how the brain perceives, learns, and produces behavior, and how neural disorders disrupt normal cognitive processing. The goal of this proposal is to address this requirement by developing a publicly available set of inference algorithms for deciphering information flow networks in the brain, using the songbird vocal communication system as our testing and experimental model. Songbirds are one of the only accessible non-human animals where learned vocal communication, the substrate for human language, can be studied. Non-human primates, rodents, and other commonly studied animals do not have this ability. Using multielectrode array electrophysiology data from songbirds, the PIs and their colleagues have recently developed new computational methods for automatically inferring models of neural flow networks. Here, electrophysiology data will be collected from the auditory and vocal pathways of the songbird brain and provided to our new computational inference methods, in order to automatically infer the architecture of the neural flow networks that arise and evolve during auditory and vocal learning. With this tool, we can study the network mechanisms of neural deterioration of learned vocalization that occurs due to deafening, as in humans; we can study basal ganglia disorders that affect learned communication-including stuttering—thus gaining better insight into treating auditory, vocal, and mental disorders. The results will allow the PIs to formulate and experimentally test models that describe how vocal learners learn to recognize and vocalize the sounds they hear in their environment. The proposed methods will enable investigators to monitor-in near real time—how different regions of the brain exchange information during various processing and learning tasks. The proposed algorithms are applicable to a wide range of biological (and non-biological) problems. Any neural system can be studied and the methods can be applied to a range of different types of data, e.g. single or multi-unit recordings, EEG, or fMRI. To facilitate this, an entire aim of the proposal is dedicated to producing userfriendly software of high quality and modularity for general use throughout the neuroscience and general science communities. This will enable scientists to better understand how neural anatomical networks are actively utilized and how that utilization evolves over time.

Project (or PI) websites

http://www.cs.duke.edu/~amink

http://www.jarvislab.net

Publications

1. Smith, V., Yu, J., Smulders, T., Hartemink, A., & Jarvis, E. (2005) "Computational Inference of Neural Information Flow Networks." *(submitted)*.

Before receiving the CRCNS grant, we published a number of articles on related topics that laid the foundation for our proposal. Below is a selection:

- 2. Hartemink, A. (2005) <u>"Reverse Engineering Gene Regulatory Networks."</u> *Nature Biotechnology*, **23**, May 2005. pp. 554–555.
- Bernard, A. & Hartemink, A. (2005) <u>"Informative Structure Priors: Joint Learning of Dynamic Regulatory Networks from Multiple Types of Data."</u> In *Pacific Symposium on Biocomputing 2005 (PSB05)*, Altman, R., Dunker, A.K., Hunter, L., Jung, T., & Klein, T., eds. World Scientific: New Jersey. pp. 459–470.
- 4. Yu, J., Smith, V., Wang, P., Hartemink, A., & Jarvis, E. (2004) <u>"Advances to</u> <u>Bayesian Network Inference for Generating Causal Networks from Observational</u> <u>Biological Data."</u> *Bioinformatics*, **20**, December 2004. pp. 3594–3603.
- Smith, V., Jarvis, E., & Hartemink, A. (2003) <u>"Influence of Topology and Data Collection on Functional Network Inference."</u> In *Pacific Symposium on Biocomputing 2003 (PSB03)*, Altman, R., Dunker, A.K., Hunter, L., Jung, T., & Klein, T., eds. World Scientific: New Jersey. pp. 164–175.
- Yu, J., Smith, V., Wang, P., Hartemink, A., & Jarvis, E. (2002) <u>"Using Bayesian Network Inference Algorithms to Recover Molecular Genetic Regulatory Networks.</u>" International Conference on Systems Biology 2002 (ICSB02), December 2002.
- Jarvis, E., Smith, V., Wada, K., Rivas, M., McElroy, M., Smulders, T., Carninci, P., Hayashisaki, Y., Dietrich, F., Wu, X., McConnell, P., Yu, J., Wang, P., Hartemink, A., & Lin, S. (2002) <u>"A Framework for Integrating the Songbird Brain."</u> *Journal of Comparative Physiology A*, 188, December 2002. pp. 961–980.
- 8. Smith, V., Jarvis, E., & Hartemink, A. (2002) <u>"Evaluating Functional Network</u> <u>Inference Using Simulations of Complex Biological Systems.</u>" Intelligent Systems in Molecular Biology 2002 (ISMB02), *Bioinformatics*, **18:S1**. pp. S216–S224.
- Hartemink, A., Gifford, D., Jaakkola, T., & Young, R. (2002) <u>"Combining Location and Expression Data for Principled Discovery of Genetic Regulatory Networks."</u> In *Pacific Symposium on Biocomputing 2002 (PSB02)*, Altman, R., Dunker, A.K., Hunter, L., Lauderdale, K., & Klein, T., eds. World Scientific: New Jersey. pp. 437–449.

Hartemink, A. (2001) <u>"Principled Computational Methods for the Validation and Discovery of Genetic Regulatory Networks.</u>" Massachusetts Institute of Technology, Ph.D. dissertation.