

Biological Physics Theory Unit (Greg Stephens)

FY2018 Annual Report

Biological Physics Theory Unit

Professor Greg J Stephens



Abstract

The Stephens Group is pioneering a new field – the physics of behavior: from individual organisms to entire societies. The science of the living world is overwhelmingly focused on the microscopic: the structure of DNA, the machinery of cells that can convert energy and transports materials, or the pattern of electrical activity in our brains from which thoughts arise. Yet, all of these processes serve the greater evolutionary goals of the organism: to find food, avoid predators and reproduce. This is the behavioral scale, and despite it's importance, our quantitative understanding of behavior is much less advanced. But how do we quantify the emergent dynamics of entire organisms? What principles characterize living movement? Research in our group addresses these fundamental questions with a modern biophysics approach and model systems ranging from the nematode *C. elegans* to zebrafish

and honeybee collectives. We combine theoretical ideas from statistical physics, information theory and dynamical systems and work in close collaboration with scientists from OIST and around the world to develop and analyze novel, quantitative experiments of organisms in natural motion.

1. Staff

- Prof. Greg J. Stephens
- Ms. Naoko Ogura-Gayler, Research Administrator
- Dr. Kasia Bozek, Group Leader
- Ms. Laetitia Hebert, Software Engineer
- Mr. Tatsuo Izawa, Technician
- Mr. Yoann Portugal, Technician (from Jan 2019)
- Mr. Tosif Ahamed, PhD Student
- Mr. Liam O'Shaughnessy, Visiting Research Student
- Mr. Antonio Carlos Costa, Visiting Research Student
- Mr. Xavi Fernandez-Luengo Flores, Research Intern

2. Collaborations

2.1 Human Frontiers Science Program

- Description: The physics of social behavior in the 3-dimensional shoaling of zebrafish, *Danio rerio*
- Type of collaboration: Joint research
- Researchers:
 - Professor Ichiro Masai, OIST Graduate University, Okinawa JP
 - Professor Joshua Shaevitz, Princeton University, Princeton USA

2.2 Information Processing in Living Systems

- Description: Theoretical Biophysics of Optimal Sensing
- Type of collaboration: Joint research
- Researchers:
 - Dr. Vudiwat Ngampruetikorn, Northwestern University, Evanston USA

3. Activities and Findings

3.1 Research Findings and Activities

In FY2018 the Biological Physics Theory group continued to advance in methodological development for the high-resolution posture-scale 3D tracking of multiple zebrafish (Figure 1) and in building markerless detection and tracking techniques to capture the individual dynamics of every bee in a large colony (Figure 2). Theoretical and computational work on understanding complex dynamics, with a focus on approaches rooted in dynamical systems and statistical physics, resulted in the publication (including associated data and code) of an interpretable yet powerful locally-linear model (Figure 3).

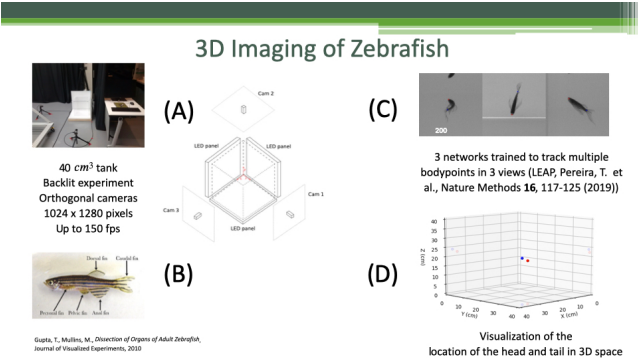


Figure 1: We continue to progress in constructing an imaging system and computational pipeline for the 3D bodypoint tracking of zebrafish.

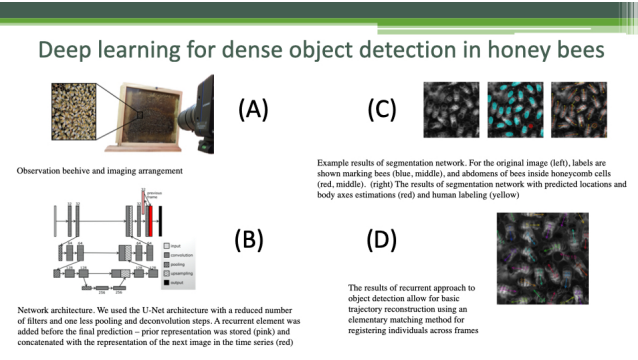


Figure 2: Our first published results using deep learning for dense object detection (Bozek et al, CVPR 2018). We aim for the markerless tracking of an entire insect colony at high temporal resolution.

Adaptive, locally-linear models of complex dynamics

Unsupervised classification of *C. elegans* posture and neural dynamics



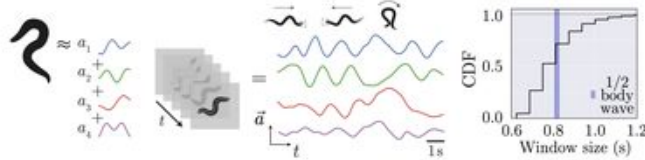
Antônio Carlos Costa¹, Tosif Ahamed² and Greg Stephens^{1,2}

¹ - Department of Physics and Astronomy, Vrije Universiteit Amsterdam, The Netherlands
² - Biological Physics Theory Unit, OIST Graduate University, Okinawa, Japan



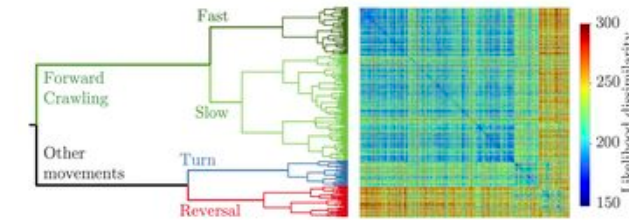
Natural phenomena are teeming with temporal complexity but such dynamics, however fascinating, offer substantial obstacles to quantitative understanding. We introduce a general method based on local linear models within windows determined adaptively from the data. To explore the resulting model space, we develop a novel likelihood-based hierarchical clustering technique and we examine the eigenvalues of the linear dynamics. Our approach identifies fine grained dynamical states in the posture and neural imaging of *C. elegans*. At the level of posture, we find model dynamics which fluctuate around the instability boundary, and we detail a bifurcation in a transition from forward to backward crawling. At the neural level, we show that the stability of global brain states changes with oxygen concentration.

Canonical posture behaviors are automatically identified



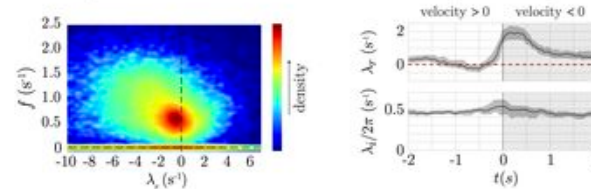
The posture dynamics is projected into a 4-dimensional time series using "eigenworms" [1].

Segmentation yields window sizes with a median that matches the duration of half a body wave.



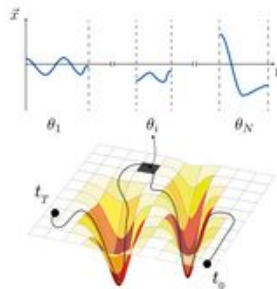
Likelihood hierarchical clustering: canonical behaviors emerge at the top levels of the tree.

Posture dynamics fluctuates around the instability boundary



Distribution of frequencies peaks at $f \sim 0.6 \text{ s}^{-1}$ (body wave frequency) and spills across the instability boundary. Hopf bifurcation occurs with reversals.

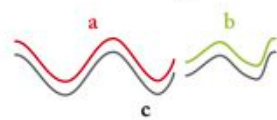
Adaptive locally-linear segmentation



A complex multidimensional time series is adaptively segmented into local linear models, using the properties of the time series itself to estimate the length of each local approximation.

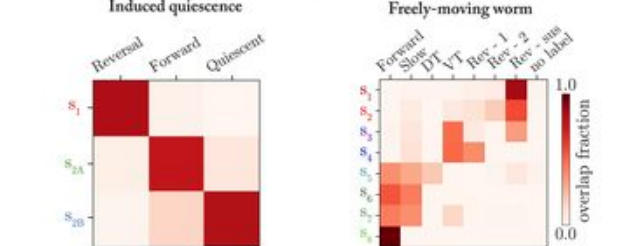
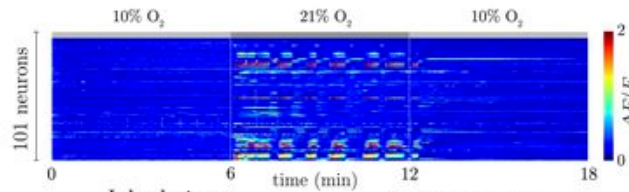
This is similar to approximating a complex-shaped manifold by a set of locally-flat patches, encoding a non-linear time series as a trajectory in the space of local linear models.

Likelihood hierarchical clustering



The dissimilarity between local linear dynamics is measured by the loss in likelihood of fitting windows **a** and **b** using the parameters estimated in the combination of windows **c**.

Whole-brain dynamical states are automatically identified

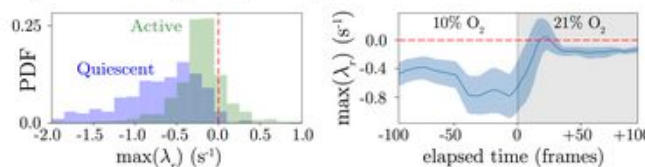


Example brain-wide fluorescence signal
 O_2 concentration changes in 6 minute periods: 10% O_2 induces a quiescent state, 21% O_2 induces an active state.

Confusion matrix is sparse: our clustering matches previous labels both in the induced quiescence experiments [2] and in freely moving worms [3].

(DT/VT - dorsal/ventral turn
 Rev-sus - sustained reversal)

Dynamical stability changes with global brain state



Quiescent states are stable; active states cross the instability boundary. Stability changes with O_2 concentration.



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arXiv:1807.09728 [q-bio.QM]



Novel general approach for the analysis of complex dynamics that yields an interpretable yet complete representation; generally applicable

Likelihood hierarchical clustering finds global dynamical patterns at multiple spatio-temporal scales; the level of description can be chosen appropriate to the nature of the analysis

Posture and neural dynamics exhibit near instability behavior

Dissimilarity measure enables comparison of dynamics across datasets: master repertoire of behaviors; variability across species or due to perturbations

References

- [1] - Stephens et al. (2008) Dimensionality and dynamics in the behavior of *C. elegans*. PLOS Comput. Biol.
- [2] - Nichols et al. (2017) A global brain state underlies *C. elegans* sleep behavior. Science
- [3] - Kato et al. (2015) Global brain dynamics embed the motor command sequence of *Caenorhabditis elegans*. Cell

Acknowledgements

This work was supported by the research programme of the Foundation for Fundamental Research on Matter (FOM), which is part of the Netherlands Organisation for Scientific Research (NWO), and also by funding from The Okinawa Institute of Science and Technology Graduate University.

Figure 3: Our approach for analyzing complex, multidimensional time series using interpretable, locally-linear models applies across a wide variety of systems, from the motor behavior of *C. elegans* to neural dynamics and more (Costa et al, PNAS 2019).

3.2 Professional Activities

GJ Stephens, Co-organizer, Physics of Behavior: Movement, Control, and Learning, Aspen Center for Physics, USA May 27-June 17 (2018)

GJ Stephens, Co-director, Cajal Course in Behavior of Neural Systems, Lisbon, Portugal July 15-Aug 4 (2018)

3.3 PhD Dissertations

Ray Xin Lee (Supervisor: Bernd Kuhn; Co-supervisor: GJ Stephens; Mentor: Mukhles Sowwan)
Thesis Title: Nature and source of animal spontaneous behaviors: Insights from psychobehavioral development and neuronal population dynamics in mice

OIST Graduate University <http://doi.org/10.15102/1394.00000700>

Hiroaki Hamada (Supervisor: Kenji Doya; Co-supervisor: GJ Stephens)

Thesis Title: Serotonergic Control of Brain-Wide Dynamics

OIST Graduate University

4. Publications

4.1 Journals and Preprints

1. A Carlos Costa, T Ahamed & GJ Stephens, Adaptive, locally-linear models of complex dynamics. Proc Nat Acad Sci (USA) 107, 14425–14430 (2019); arXiv:1807.09728 [q-bio.QM].
2. K Bozek, L Hebert, AS Mikheyev & GJ Stephens, Pixel personality for dense object tracking in a 2D honeybee hive. (2018); arXiv:1812.11797 [cs.CV].
3. RX Lee, GJ Stephens & B Kuhn, Affective bonding explains post-traumatic behavioral development in adult mice. (2018); bioRxiv:249870.
4. K Bozek, L Hebert, AS Mikheyev & GJ Stephens, Towards dense object tracking in a 2D honey- bee hive. IEEE/CVF Conference on Computer Vision and Pattern Recognition 4185–4193. (2018); doi:10.1109/CVPR.2018.00440; arXiv:1712.08324[cs.CV]

4.2 Books and other one-time publications

Nothing to report

4.3 Oral and Poster Presentations

1. GJ Stephens, American Physical Society Meeting Session R51: Artificial Intelligence, Data, and Dynamics: Learning Physical Models of Living Systems, Boston US (Mar 2019)
2. Kasia Bozek, Max-Delbrück Center for Molecular Medicine, Berlin DE (Nov 2018)
3. GJ Stephens, University of Konstanz, Konstanz DE (Nov 2018)
4. GJ Stephens, Informatics Seminar, University of Sussex, Brighton UK (Nov 2018)
5. GJ Stephens, OIST Faculty Lunch (Oct, 2018)
6. GJ Stephens, Banbury Meeting on Quantitative Approaches to Naturalistic Behaviors, Cold Spring Harbor US (Sep 2018)
7. A Costa*, T Ahamed & GJ Stephens, Physics of Living Matter XIII, Marseille FR (Sep 2018)
8. GJ Stephens, FENS Forum on Using Computational Neuroethology to Dissect the Neural Basis of Behavior, Berlin DE (Jul 2018)

9. GJ Stephens, OIST Computational Neuroscience Course, Okinawa Japan (Jun 2018)
10. GJ Stephens Physics colloquium, University of Oregon, Eugene US (Jun, 2018)
11. K Bozek*, L Hebert, AS Mikheyev & GJ Stephens, Conference on Computer Vision and Pattern Recognition (CVPR), Salt Lake City, US (Jun, 2018)

5. Intellectual Property Rights and Other Specific Achievements

Nothing to report

6. Meetings and Events

Seminar

6.1 Mapping the Structure of Animal Behavior

- Date: Dec 17, 2018
- Venue: OIST Campus Lab 1
- Speaker: Prof. Gordon Berman, Emory University

6.2 Evolutionary predictions from biophysical models by Prof. Michael Laessig, University of Cologne

- Date: July 15, 2018
- Venue: OIST Center Building
- Speaker: Prof. Michael Laessig, University of Cologne

Meeting at OIST

- Date: November, 2018
- Venue: OIST Lab 2
- Speaker: Prof. Joshua W. Shaevitz, Princeton University

Meetings, Travel

- Physics of Behavior: Movement, Control, and Learning, Aspen Center for Physics, Aspen USA (Jun 2018)
- 13th International Zebrafish Conference, Madison USA (Jun 2018)
- Meeting with Prof. Tim Landgraf, Freie Universitat Berlin, Berlin DE (Nov 2018)
- Meeting with Prof. Ben de Bivort, Harvard University, Cambridge USA (Mar 2018)

7. Other

Nothing to report.