Complex computation in biological systems

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A bit about me...

- Bsc, Applied Physics, Columbia University, New York
  (concentration, quantum electronics)
- MSc, Physics, Technion Israel Institute of Technology, Haifa
  (topic: theoretical quantum optics)
- PhD, Physics (2000), Technion Israel Institute of Technology, Haifa
  (topic: biological physics, experiment + theory)
- Postdoc, Zoology, Biomathematics, Physics, Tel Aviv University
  (topics: human genome, mathematical immunology, neuroscience

- In Leeds since 2002 (Lecturer → Reader → Chair).
  EPSRC Fellowships:
  - Advanced Research Fellowship (2005)
  - Leadership Fellowship (2011)

Track record *ca.* 2004: Strongest publications in Physics journals, too few in biology. Co-organised EPSRC Network on “complex networks”; Leeds PI on two large (>£1M) multi-institutional projects on complexity.

Why study biological systems?

Biological computation is complex

molecular
cellular
network
system
environment

robustness
emergence

Can we understand the organisation of function in nervous systems and in the brain?

- How does function emerge?
- What makes it robust?

Can problems be decomposed into “modules” and can we relate the mathematical decomposition to observable properties of neurons and networks?

Can we identify molecular/cellular mechanisms as *building blocks* of computation?

Can we understand the emergence of function in terms of hierarchies of building blocks?

(… before Leeds)

A reductionist approach:
Pinning down computation in neural networks
2 minimalistic models of a brain

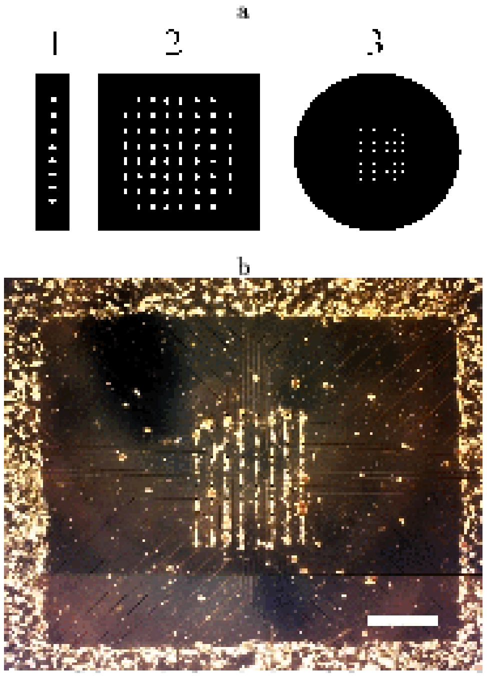
Hard-wired invertebrate networks

Small, relatively simple nervous systems with well-defined units, well-defined circuitry, and well-defined function

Random cell networks *in vitro*

Two-dimensional neural network under well-defined control conditions, with random circuitry, and self-organised/emergent function

Random networks



Cortical networks on a dish - lost morphology
lost circuitry
memory of function

- Comprehensive approach: study development & activity
- Seek universal and robust features (e.g. as function of scale)
- Study minimal forms of learning, memory and computation

The other extreme

The C. elegans locomotion nervous system

The worm

- Among the “simplest” animals
- Under 1,000 cells, 301 neurons: hard wired & completely mapped anatomy & nervous circuitry
- Modular nervous system, e.g., 64 locomotion neurons
- Forward locomotion: relatively simple task: generation and propagation of undulations. Well understood in other animals.

Trigger for fellowship
Bryden and Cohen (2004)

In *C. elegans*, sensory input, rather than central pattern generation, appears to underlie forward locomotion control.

Breadth of research programme

Experimental studies of the worm

Systematic behavioural studies

Imaging of neuronal / muscle activity

Modeling, testing and cross-validating

Mathematical & simulation modeling

Bio-mimetic robot implementation and testing

Risks and Reward

Experimental work packages

Behaviour:
- Set up “wet” lab
- Experimental track record
- Inst. Support.
- Backup: collaorate

Imaging: High reward, high risk. Follow-on from mini $6K preliminary project.

Modeling, testing and cross-validating

Modeling
- Least exciting to EPSRC
- Core to me

Integration/Management
- Build/Lead substantial multidsciplinary group
- Impact to ICT/Complexity Science/Engineering
- Gain leadership skills/ position

Bio-mimetic robot
- 0 track record
- Add value but minimise risk to overall project

Expected outcomes

- Integrated understanding of the *C. elegans* forward locomotion system
- Understanding of the integration of neural control, locomotion mechanics, and interaction with the environment in a biological and a bio-mimetic system
- Development of a novel quantum-dot based imaging technology for voltage sensing in biological cells

Long term goals

- Integrated understanding of the *C. elegans* behaviour: the simplest animal that can be modelled in its entirety.

- A step change in our understanding of a complex system and the development of appropriate research tools and methodologies to tackle it.

- Leadership...

Achievements

- Set up successful lab. 11 members at peak.
- Ticked all objectives across four WPs.
- Integrated understanding of the *C. elegans* forward locomotion: reverberated area and broadened interest to other disciplines.
- Increased recognition of the importance of physics, quantitative approaches, data analytics, computational/simulation modeling and theory.
- Established/recognised internationally in field
- Leadership (Chair by end of Fellowship)
- New questions, more focused. More challenging led to followup fellowship application (Whole Animal Modelling)

Thanks to...

- EPSRC
- Leeds Uni/School of Computing
- My lab and colleagues
- The worm

Engineering and Physical Sciences Research Council

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