Transdisciplinary Research Involving Systems Engineering and Computational Neuroscience

Opportunities and Challenges

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Aim

- Enthuse:
  - systems engineers to work with biologists;
  - biologists to work with systems engineers.
- Explain:
  - what transdisciplinary research truly is;
  - what systems engineering can bring to biology;
  - what biology can bring to systems engineering;
  - several research avenues worth pursuing.
- Generate:
  - discussion;
  - ideas;
  - collaboration.

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(The only mention of EEG in this talk is here.)

Engineering

- Engineers build and invent things (systems).
- But this involves studying how systems work and understanding theoretical strengths and limitations of system performance.
- Hence the intersection with neuroscience.
- National Academies of Engineering identified 14 Grand Challenges for this century.
  - Without appropriate leadership, these problems won't be solved.
  - These challenges are game changers.
- One of these challenges is to reverse-engineer the brain.

14 Grand Challenges of this Century for Engineers

Make solar energy economical
Provide energy from fusion
Develop carbon sequestration methods
Manage the nitrogen cycle
Provide access to clean water
Restore and improve urban infrastructure
Advance health informatics
Engineer better medicines
Reverse-engineer the brain
Prevent nuclear terror
Secure cyberspace
Enhance virtual reality
Advance personalized learning
Engineer the tools of scientific discovery

Reverse-engineering the Brain

To reverse-engineer the brain, we argue the four overarching and integrated goals should be to:

- Discover the mathematical principles which explain how the brain works and underlie its neural organisation and function.
- Develop multi-scale computational models of the brain based on biophysical principles and that have experimentally validated predictive power.
- Develop pioneering techniques for better interfacing to neuronal circuitry and use these methods in experiments for model validation and refinement.
- Produce *transdisciplinary* scientists whose knowledge spans areas of the life sciences, physical sciences and engineering.

Quote by Norbert Wiener — 1/3

Norbert Wiener, the founder of cybernetics, wrote that it is the:

boundary regions of science which offer the richest opportunities to the qualified investigator. They are at the same time the most refractory to the accepted techniques of mass attack and the division of labor.

- Divide-and-conquer does not work.

Quote by Norbert Wiener — 2/3

Wiener went on to explain that

> a proper exploration of these blank spaces on the map of science could only be made by a team of scientists, each a specialist in his own field but each possessing a thoroughly sound and trained acquaintance with the fields of his neighbors; all in the habit of working together, of knowing one another's intellectual customs, and of recognizing the significance of a colleague's new suggestion before it has taken on a full formal expression.

- Breadth of knowledge is required because ideas still come from individuals (the team helps align thought processes).

Quote by Norbert Wiener — 3/3

Wiener clarified that:

The mathematician need not have the skill to conduct a physiological experiment, but he must have the skill to understand one, to criticize one, and to suggest one. The physiologist need not be able to prove a certain mathematical theorem, but he must be able to grasp its physiological significance and to tell the mathematician for what he should look.

Macy Conferences

- Macy conferences (1946–1953).
- Aimed for a general science of the workings of the human mind.
- One of the earliest organised approaches to transdisciplinarity.
- Attracted leading scientists from across engineering (e.g., Wiener, von Neumann and Shannon) and the physical and life sciences.
- Demonstrated the need for, and initial difficulties in, establishing a common language powerful enough to communicate the intricacies of the relevant fields across the physical and life sciences and engineering.
- Insufficient experimental data prevented continuation.
- (We are now data rich.)

Past Breakthroughs

Breakthroughs originally came from better measurement equipment that afforded a competitive edge.

- Nobel prize (1963):
    - Jack Eccles (Australian National University);
    - discovered chemical means by which impulses are communicated or repressed by neurons;
    - worked closely with Jack Coombs, formerly a professor of engineering at Dunedin.
- Nobel prize (1970)
    - Bernard Katz;
    - studied chemistry of synaptic transmission;
    - formerly a radar officer in the RAAF.

The Present

- Progress still being made via better equipment and ingenious experiments. (Optical is “superseding” electrical measurements.)
- Engineering has *supported* neuroscience (e.g., equipment).
- Engineering has *borrowed* from neuroscience (e.g., artificial neural networks).
- Engineering has *lent* some mathematical tools to neuroscience (e.g., information theory).
- But this is not transdisciplinary research.
- There has not been a return to the “Macy conference era”.

The Future

- The future is a symbiotic relationship involving mathematics, engineering and biology.
- Boundaries will blur.
    - Neuroscientists will be trained in systems engineering.
    - Engineers will be trained in neuroscience.
- Recent national reports (USA, UK) foresee this.
- The Macy conferences foresaw this over half a century ago!
- It seems clear this is the best approach.

Symbiotic Relationships

- The last century saw an extremely productive symbiosis between mathematics and physics.
- It demonstrates how “theory” and “practice” propel each other.
- The remainder of this presentation will examine how systems engineering and computational neuroscience can grow together.

Holistic versus Reductionist

- Different disciplines approach similar problems differently.
- Neuroscientists tend to take “reductionism” to mean the starting point is to understand the role of every molecule in a neuron.
- “We need to celebrate the equally vital contribution of those who dare to take what I call *a crude look at the whole*.” — Murray Gell-Mann, Nobel Laureate in Physics, 1994.
- Multi-scale modelling links “understanding the individual pieces” with “understanding the whole”.
- Everyone claims to be doing multi-scale modelling, but are they?

A Key Challenge in Neuroscience

- Models exist at different levels, for example:
  - sub-cellular processes;
  - single neurons and micro-circuits;
  - pathways (auditory, visual).
- But currently there are not any true multi-scale models because no one can link the models across scales.
- No one knows what the essential features are at one scale that are required to predict behaviour at another scale.

Multi-scale Modelling

- Multi-scale modelling is the field of solving physical problems which have important features at multiple scales, particularly multiple spatial and/or temporal scales.
- It seeks to predict system behaviour based on knowledge of the atomistic structure and properties of elementary processes.
- Traditional monoscale approaches are infeasible for such problems.
- The key is to work out how to link the scales.
- How to construct multi-scale models?
    - Neuroscientists: generally bottom-up.
    - In other areas: top-down (but with some bottom-up influence).

Meteorology

- Weather forecasting is an example of multi-scale modelling.
- The most challenging task is modelling the interaction between sub-systems of different spatial and temporal scales.
  - A Global Climate Model typically has about a 100km grid size.
  - Cloud structure is of the order of 0.5km.
- Experience demonstrates that bottom-up does not work.
- Improving the modelling of a process at one scale can actually make the overall model worse, not better.

Prediction 1

- Understanding the brain will be achieved most efficiently via a genuine multi-scale modelling approach.
- Success will require a “systems perspective” just as much as it will require biological insight.
- An engineering viewpoint will lead to a structured and holistic approach for determining what experiment to perform next (via suitably augmented theories of system identification and model validation).

No Panacea

- Engineering is not a panacea because current engineering theories are insufficiently advanced to be immediately applicable to biological systems.
    - Engineers do not yet understand how massively interconnected systems work (even systems they designed themselves!).
    - Cannot apply formulae from information theory to neuroscience data and *a priori* expect the answer to be meaningful.
- The methodology is correct nonetheless.
- Just as mathematics grew with physics, now engineering must grow with biology.

Prediction 2

- Systems engineering principles will expand to encompass biological systems.
- These expanded principles will ultimately explain how the brain works.
- They will also lead to better engineered systems.
  - Biological systems outperform engineered systems by many orders of magnitude (ratio of performance to energy consumption).

Kandel

- Eric Kandel was a recipient of the 2000 Nobel Prize for his research on the physiological basis of memory storage in neurons.
- He worked with Aplysia (large sea slugs).
- He was initially strongly discouraged (including by Eccles!).
  - The existing hierarchy of acceptable research questions in neurobiology meant few self-respecting neurophysiologists would leave the study of learning in mammals to work on an invertebrate.
  - Some very knowledgeable psychologists were sincerely skeptical that anything interesting about learning and memory could be found in a simple invertebrate animal.
- This mentality still exists to some extent today.

Prediction 3

- A broader perspective is required.
- Study simpler systems.
    - C. elegans (only 302 neurons).
- Understand principles behind:
    - evolution (how did life begin?);
    - systems biology (how do molecules compute?).
- Study different architectures for computation:
    - analogue computation;
    - stochastic computation;
    - effect of structure (topology) on stability and fault tolerance.
- The above all give clues as to how the brain works.
- Complex problems are solved by chipping away at them in many different places at once.

Conclusion

- Different disciplines approach problems differently.
- This century will see a convergence of the physical and life sciences.
- Transdisciplinarity will play a key role in solving complex problems.
- This will lead to the best of all worlds.