Top Priority Idea

Neuroscience, from Molecules to Mind

How do the brain and the mind function?

What is a memory? When thinking about a loved one...how is that represented at a cellular and a molecular level? How is our brain biology established so that we can perceive the world around us, and what happens in neurodevelopmental disorders like autism and mental retardation? In devastating diseases like Alzheimer’s, where humanity is slowly drained through the loss of memories, what is it that is being damaged and how can it be repaired? Understanding the nervous system will reframe how we think about cognition, memory and mental disease. Answers to these questions remain some of the great intellectual challenges of our time, and Yale is uniquely positioned to lead in answering them.

How does a brain self-assemble during development? A healthy human brain has ~100 billion neurons and over 80 trillion synaptic connections: more neurons than there are stars in the Milky Way. Proper wiring of these 100 billion neurons is necessary for the normal functioning of the human brain, and erroneous connections lead to neurodevelopmental disorders and disease. How the interconnectedness of 100 billion cells that underpin human behavior is coordinated during development is a grand challenge to understand.

What are the bases for complex human thought, emotion, language, and social behavior? Today, we view the brain as the core element of human identity, and understanding it has broad implications ranging from medicine to law. Abstract thinking, language and social behaviors are some of the most distinctive aspects of being human. While many neuroscientists study the human brain and cognition, understanding what makes brains unique is not typical of neuroscience research institutions. Understanding the conserved traits necessary for brain function, as well as the traits that make different animal brains unique is a fundamental question in neuroscience that, if developed here, will uniquely position Yale in the field.

What goes wrong in neurodevelopmental, neurodegenerative, and psychiatric diseases? As many as 100 million Americans are afflicted by at least one of the more than 1,000 known neurological diseases. The economic burden of these diseases is estimated to be over $800 billion. As the population continues to age, these numbers continue to increase. Many of these diseases lack modifying therapies or cures. Yale is well-positioned to build on the formidable strength of its basic research and clinical departments to shed new light on the fundamental mechanisms that underlie neurodevelopmental, neurodegenerative and psychiatric diseases. This could be done by linking existing strengths and fostering collaborative relationships that translate this knowledge into impactful treatments of diseases and disorders of the brain and the nervous system.

Neuroscience is composed of many disciplines that work across multiple scales, ranging from psychology to structural biology. These disciplines use distinct approaches to address the same fundamental questions, and until recently, the approaches could not be cross-referenced because of differences in the scale of the problems being examined. Advances in molecular, cellular and functional brain imaging, remarkable progress in whole-genome sequencing and gene editing techniques, plus innovative methods in theory, modeling, machine learning, and statistics, have changed the way neuroscientists analyze and understand complex brain functions across scales. These advances have opened new opportunities to address the grand challenges in neuroscience—the key to which is bringing these diverse fields together.

Vertical advances in science result from the collision of traditionally separate fields, catalyzed either by the integration of multidisciplinary approaches that produce new knowledge or by the development of new
tools that allow conceptual reframing of fundamental problems. The neurosciences are about to experience such a vertical leap, and Yale should position itself to lead.

**Raising Yale’s profile in the neurosciences**

Yale boasts some of the world’s leaders in the fundamental biology of the nervous system as well as neuropsychiatric disorders, nervous system development, neurosurgery, cognition, learning and memory, genetic discovery, and much more. Yale leads both in the development and implementation of emerging technologies—imaging in particular, including functional MRI for real-time brain imaging and super-resolution microscopy for discovery at molecular scales. Yale therefore has, distributed across a broad footprint, all the necessary ingredients to catalyze integrative approaches with transformative consequences for our understanding of cognition and perception, memory and plasticity, and the genetic and cellular mechanisms that underlie nervous system disease and dysfunction.

Yet, the current organization of neuroscientists at Yale is not aligned with these exciting opportunities. It is instead arranged based upon the history of the field at Yale. Therefore, as good as we are individually, Yale lacks a single integrative entity in the neurosciences. This gap puts Yale at a competitive disadvantage in research, clinical activity and funding. There is a need to better organize ourselves, to establish a nucleating entity in neuroscience that will drive innovation and push the boundaries of neuroscience research—which in turn will help attract government support and philanthropic contributions. To address this critical shortcoming, Yale should integrate the outstanding (but dispersed) intellectual, academic, and clinical resources across the neurosciences on campus into a broader organizational framework, the Yale Neuroscience Institute.

Examples abound of the problems that can be addressed by such an integrated approach to Neuroscience. An explanation of network and cognitive dysfunction in Alzheimer’s Disease will require input from scientists with expertise in molecular, cellular, systems, genetic, structural biological, immunobiological, imaging, psychiatry, and pharmacology. Understanding the causes of neurodevelopmental disorders like autism will similarly require input from scientists in molecular genetics, cellular biology, developmental biology, physiology and cognition. Both of these examples are representative of how challenges in neuroscience need to be addressed, and how they will require coordination across scales, and research that crosses traditional disciplinary boundaries to achieve the necessary outcomes.

Neuroscience at Yale, broadly conceived and interdisciplinarily organized, would be ideally positioned to address the biggest questions in Neuroscience. What are the mechanisms of neurological disease and dysfunction? What is the bases for neurological development, learning, memory, and plasticity? What constitutes cognition and perception? What is unique about the human brain? How can machine learning and artificial intelligence inform us about our own learning and our own intelligence?

**To advance University-wide efforts in Neuroscience, we offer the following recommendations:**

- **Organizational Structure**: The University should establish a single, integrated Neuroscience Institute to serve as a “home” and intellectual convening point for the neurosciences at Yale across all its scales and disciplines.
  - The Yale Neuroscience Institute must be interdisciplinary and cross-campus, integrating research in the biomedical sciences, clinical programs, psychology, engineering and data science. It needs to incorporate Yale’s strengths in neurological, neurodegenerative, neuropsychiatric, and neurodevelopmental diseases as well as imaging from molecule to mind.
The governance structure of this Institute should consist of a director or a small number of co-directors that represent basic and clinical science, the various schools, and the different levels of neuroscience inquiry (molecules to minds). The director(s) would be advised by a steering committee that further broadens representation.

Context for the framework of the Institute could be drawn from existing successful centers with a split academic/translational research mission, such as the Yale Cancer Center, with its strong focus, clear administration, support mechanisms, core facilities, and physical space.

The Institute should include faculty from multiple departments across FAS, YSM, including the departments in which neuroscience-related research is taking place. A subset of these faculty would be physically housed within Institute space.

- **Space:** The University should identify a dedicated space of sufficient size to house 35-40 research groups. There should also be sufficient space to convene students and faculty from the larger neuroscience community to participate in Institute functions.
  - The space should be located between the Medical School and Central Campus to facilitate cross-communication between basic science faculty and researchers in clinical departments.
  - Faculty who are physically housed within the Institute should have primary appointments in FAS and/or YSM departments. The Institute should not be the domain of a single school or department.
  - Given the large scale of neuroscience research underway at Yale, not everyone engaged in neuroscience research needs to be, should be, or even can be, physically co-located.
  - The Institute space should include seminar rooms, meeting spaces, core facilities and hoteling offices needed to convene the larger neuroscience community.
  - There is a need for vivarium space to support the neuroscience research enterprise, and this space should be in close proximity to the Institute space.

- **Faculty:** We recommend that the University perform a comprehensive review of its faculty strengths in the Neurosciences and identifies areas where faculty appointments could bolster current weakness or capture future opportunities. Three potential areas of interest are: theoretical neuroscience, disease modeling, and artificial intelligence/machine learning (see Data Science above).
  - New hires should address these opportunities using currently committed hiring resources and/or incremental slots.
  - Faculty hired into the Neuroscience Institute should have faculty appointments in FAS and/or YSM departments. Faculty hired into any incremental slots should be identified through a joint search committee process.

- **Students:** The Institute should become the home for the INP (Interdepartmental Neuroscience Program). An exceptionally deep pool of quality students applies to the INP. Given the quality of the student pool, the number of faculty in neuroscience, and the high placement rates of graduating students, an increase in the INP size is justified, possibly by as much as twice the current size.

- **Core facilities:** We recommend facilitated, expanded and improved access to key core facilities, including new and existing cores that support the research enterprise and promote collaborative interactions (see Core Facilities recommendation above).
• **Education**: The Neuroscience Institute should be a home for interdepartmental teaching and training initiatives at the undergraduate, graduate, and postdoctoral levels.

  o We recommend that Yale continue to promote the new undergraduate Neuroscience major, utilizing the resources of FAS and YSM faculty for its instruction and research training. The convening role played by this Institute will be a strong asset to the teaching initiative.

  o Graduate trainees would benefit from the opportunity afforded by the Institute to engage in research across scales from molecules to the mind and establish collaborations between faculty.