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Building a Wiring Diagram of the Human Brain

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In biology, structure and function are inextricably linked. Much of neuronal function is determined by anatomical connections—the brain's 'wiring diagram.' Moreover, most brain disorders are understood to be problems not confined to the cells of a particular region, but distributed through the communication among multiple brain regions. Thus, they are essentially connectionist disorders. My laboratory's ultimate goal is to build the wiring diagram of the human brain. However, this is not a straightforward task: the gold standard for assessing anatomical connectivity, tract-tracing, is not possible in humans, and requires combining across brains to infer whole-brain connectivity. Other methods are either post-mortem (label-free optical imaging) and/or non-invasive (diffusion MRI); however, these have their own challenges with resolution and accuracy.

I will highlight how deliberately cross-species and cross-modal pipelines can help us achieve more accurate wiring diagrams of the human brain. These diagrams can aid us in neuromodulation and provide us with the neuroanatomical underpinnings of complex behaviors and resting-state fMRI results. Finally, I will describe the use of connectivity as a defining metric of brain regional similarity across species, including rodents. The coming years will require comparing connectivity maps across nonhuman animals and humans to establish translational value.