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Bayesian approach to behavior mapping and complex decision, the *Drosophila* larva

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computational tools and experimental protocols needed to control this system; principally the relationship between the Gaussian curvature and the reaction phase, and optical imprinting of the wave pattern. Finally, we present our current journey towards autonomous soft swimmers.

Together, these results demonstrate a route for modeling and developing fully autonomous soft machines mimicking some of the locomotive capabilities of living organisms.

Platform: Neuroscience

744-Plat

Morphological and molecular diversity of human astrocytes in a cerebral organoid

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Astrocytes are a type of glial cell in the central nervous system responsible for modulating synaptic transmissions, tissue repair, maintaining homeostasis, and are therefore implicated in many neurological diseases. Historically, cortical astrocytes were assumed to be a homogeneous population; however, it has recently been demonstrated that there is both morphological and transcriptome heterogeneity between cortical layers, implying diverse functional capacities and responsibilities. Human astrocytes are also more structurally complex, larger, and have unique subtypes in comparison to the commonly studied rodent astrocytes. Interestingly, one of these subtypes, the interlaminar astrocyte, has also been reported to express various proliferation markers. As access to human cortical tissue is sparse, emerging cerebral organoids derived from human stem cells have become a popular *in vitro* model for studying the human cortex. Astrocyte subtypes unique to humans have been recapitulated in a sliced cortical organoid model, but have not been quantitatively characterized. Here, we have characterized various GFAP expressing populations in cerebral organoids based on morphology, spatial distribution, and expression of astrocytic and proliferation markers. Establishing astrocyte morphologies and molecular profiles in a cerebral organoid model is an important step in understanding the diverse functions of astrocytes in a human context.

745-Plat

In situ structural biology of pathological protein deposits in Alzheimer's disease

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Fibrillar aggregates of A β peptides and tau protein are defining features of Alzheimer's disease (AD) and evidence is accumulating that peptide conformation within fibrils correlates with disease subtype. Nevertheless, high resolution structures of fibrillar polymorphs fall short of defining the molecular mechanisms underlying disease. Mapping of the spatial distribution of polymorphs at multiple length scales—within plaques and tangles, across brain tissue, and in multiple brain regions—is being carried out to supplement high resolution information. X-ray scanning microdiffraction and IR microscopy of thin sections of human brain tissue are being used in conjunction with immunohistochemistry of serial sections to extract structural information of sufficiently high resolution to determine, *in situ*, the distribution of distinct structural forms of A β peptides in plaques and tau proteins in neurofibrillary tangles. Analysis of small-angle scattering from these lesions is being used to generate information on the size and shape of the constituent fibrils. Wide-angle scattering and hyperspectral IR microscopy are producing data relevant to the peptide fold within these structures. Combined with images of immuno-stained serial sections, these data sets are providing a sub-cellular resolution mapping of the distribution and organization of fibrillar polymorphs within and across

plaques and tangles. Are A β fibrils with a plaque all the same polymorph? Are fibrils in adjacent plaques identical? Are there differences in tau filament structure within a single tangle? A single tissue? Answers to these questions will make it possible to distinguish prion-like proliferation of fibrillar structures from independent nucleation events. A comprehensive analysis of these data may provide a basis for testing hypotheses as to how these fibrillar polymorphs contribute differentially to disease progression.

746-Plat

Bayesian approach to behavior mapping and complex decision, the *Drosophila larva*

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Nervous systems have the ability to select appropriate actions in response to stimulations. Nevertheless, there remain large knowledge gaps in linking neural architecture to behavioral response. To understand decision-making, targeting individual neurons and having a simple read-out of their activity is crucial, and *Drosophila* larvae are ideal organisms for such an approach. To explore the relationship between neural network dynamics and decision-making in *Drosophila* larvae, we mix Bayesian induction techniques and physical modeling on biological data.

By combining video measurement experiments of larval behavior with advances in modern optogenetics that allow the activation/inactivation of individual neurons, a database of millions of larvae responding to the activation of single neurons has been constructed. Larva images, especially taken at low resolution to record large amount of them, remain ambiguous and prone to multiple artifacts which impairs behavior detection and can lead to significant uncertainties during complex consecutive sets of actions. We design a new approach that combine physics informed prior to Bayesian inference to infer the real shape of the larva and detect behavior. We demonstrate its efficiency in properly regularizing the shape of larva when performing complex maneuvers, in analyzing corrupted data and in reducing direction-based errors such as mistaken a forward and backward crawl.

Once the behaviors are properly detected and quantified, we want to detect all possible responses and modulations induced by the activation or inactivation of individual neurons. Using Bayesian program synthesis, we show we can regenerate the behavioral dynamics of millions of larvae but also detect anomalies induce by individual neurons as sequences whose probabilities diverge from the model. This new approach allows modelling complex behavior with limited & tractable sets of parameters but also detect very subtle anomalies in behavioral dynamics.

747-Plat

Computational modeling of the interactions between signaling and trafficking of AMPAR during synaptic plasticity

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AMPA, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor, is a receptor concentrated at the postsynaptic density (PSD) of dendritic spines. AMPAR is often used as a readout for synaptic plasticity since increased AMPAR density at the PSD leads to a stronger synaptic response to a stimulus while decreased AMPAR density leads to a weaker response. Changes in AMPAR density during synaptic plasticity involve numerous complex signaling pathways, many of which have been studied both experimentally and computationally. However, there are still open questions regarding how the dynamics of several key components upstream of AMPAR, including CaMKII and phosphatase dynamics, influence the mechanisms and dynamics of AMPAR trafficking. Here we construct both a deterministic compartmental ordinary differential equations model and a deterministic reaction-diffusion model of the simplified signaling network underlying AMPAR dynamics during synaptic plasticity to probe how upstream kinase and phosphatase dynamics influence AMPAR dynamics and trafficking. We find that key signaling components and trafficking mechanisms act over different timescales to modulate AMPAR density at the PSD. In particular, AMPAR temporal dynamics show two timescales associated with endo/