Spatiotemporal dynamics of epileptic seizures in larval zebrafish

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Background: Epilepsy is a prevalent neurological disorder in which the brain is predisposed to recurrent episodes of abnormal neuronal activity called seizures. There are various ways to treat epilepsy, including the use of drugs to prevent seizures from occurring or surgery to implant modulation devices. However, the effect of therapies for epilepsy are difficult to predict and hence many people do not have their seizures fully controlled. If we could better understand the reasons why seizures start, stop and spread across the brain, we would be better informed to intervene and help treat epilepsy.

From a mathematical perspective, seizures can be thought of as intermittent changes to the healthy spatiotemporal dynamics of brain activity. During seizures, recordings of brain dynamics often undergo sudden changes, for example increases in amplitude, changes in waveform and alterations to the spatial distribution of activity (or the "functional connectivity"). Mathematical tools from time series analysis can help quantify these changes in patterns and mathematical models can be fit to data in order to understand how seizures are generated and how they might be avoided.

Aim: The aim of the project is to quantify the spatiotemporal dynamics of seizures in the larval zebrafish and understand how these differ from 'normal' brain activity. Zebrafish offer the unique ability to observe the dynamics of seizure activity across the whole brain simultaneously and therefore the potential to offer unique insights. In addition to quantifying this activity the student will build mathematical models to recreate the data and hence learn how large-scale brain connectivity contributes to seizure generation, and how manipulations could alleviate seizures.

We will focus on established genetic models of epilepsy in zebrafish (e.g. specific ion channel mutants) that exhibit spontaneous seizures similar to those seen in human patients with comparable genetic epileptic syndromes.

Training: The student will be immersed in an interdisciplinary environment blending techniques and theory across Mathematics and Statistics, Computer Science and Biosciences. The student will learn *in vivo* brain imaging approaches using zebrafish, advanced analysis tools for quantification of images and time series as well as methods for building mathematical models (digital twins) of zebrafish brain dynamics. They will combine mathematical models with modern AI tools to unpick which regions of the brain, at different spatial resolutions, contribute to seizure generation, progression and termination.

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