KTH Engineering Sciences

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Postdoctoral project at Brummer & Partners MathDataLab

Autonomous learning of neural signals in bioelectronic medicine

Bioelectronic medicine is an emerging discipline that combines molecular medicine, neuroscience, engineering and computing to develop devices to diagnose and treat diseases. The discipline originates from discoveries of mechanisms for neural control of biological processes that underlie disease, and the development of devices to modulate neural circuits as therapy using electrons instead of drugs. Development of new therapies relies on detailed understanding of the molecular mechanisms of disease. Traditional pharmaceutical drugs are optimized to target defined molecular mechanisms, but often lack anatomical and cellular specificity, which inevitably causes toxicity from off-target effects. Drugs are not inherently designed to adapt to individual treatment, so both under- and overdosing are common, resulting in therapy failure or unwanted side effects. Advances in bioelectronic medicine hold promise to address some of these challenges and provide personalized treatment of disease. An overview of bioelectronic medicine is given in [1].

Neural reflexes establish homoeostasis in organ systems. Recent advances in neuroscience and immunology have revealed reflex mechanisms that regulate innate and adaptive immunity. For example, ‘the inflammatory reflex’, in which the vagus nerve plays a key role, maintains immunological homoeostasis by regulating cytokine production and inflammation. This process begins when changes in the internal milieu (e.g., blood pressure, temperature, or pH) activate visceral sensory neurons that transmit action potentials along the vagus nerve to the brainstem. IL-1β and TNF, inflammatory cytokines produced by immune cells during infection and injury, and other inflammatory mediators have been implicated in activating sensory action potentials in the vagus nerve. However, it remains unclear whether neural responses encode cytokine specific information.

The aim of this project is to investigate advanced machine learning and inference algorithms for automated detection of inflammatory events by analysis of electrical neural activity. A mathematical framework, based on machine learning, stochastic processes, and functional/harmonic analysis is required to build an artificial intelligence for efficient and automated detection and decoding of HRV recordings, electrical neural activity related to pro-inflammatory cytokines, as well as information processing and process control.

Automated identification of inflammatory activity

Recorded electrical signals from multiplexed sensor samplings and/or micro electrodes contain numerous sources of noise arising from, e.g., respiratory muscle activity, cardiac activity, and ambient electrical noise. To facilitate the analysis of large sets of recordings, automated filtering algorithms, based on dense prediction combined with models of non-stationary stochastic point processes, will be developed that can separate relevant inflammatory activity from the noise.

Decomposition and synthesis of compound action potentials (CAPs).

Insights into the information encoded in neural signatures will require targeting specific activated neurons. Features must be learned from the recordings and generalized to produce useful representations of the data. In this context, latent variable models are primary candidates for modeling. The latent variables represent higher level features or abstractions of the data and the observed data is described as a deterministic or random function of these features. By studying the CAPs arising from combinations of cytokines in different proportions we aim at identifying these latent structures that represent a decomposition of the CAPs. A further aim is to develop new clustering algorithms based on reproducing kernel Hilbert spaces and deep neural networks. In addition, we aim to build on on-going work on generative models within our group at KTH to construct generative models for neural signatures. These models will be used to gain further understanding of the patterns of CAPs as well as the generation of the electrical signals used for treatment of inflammation.

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