Session: fMRI: From Basic to Intermediate Brain Connectivity, Part 2
Title: Task-less fMRI: the phenomenon of intrinsic signal fluctuations
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* **Highlights**:
    * Spontaneous hemodynamic fluctuations display spatial and temporal structure
    * Task-free fMRI has become a powerful approach for studying properties of large-scale brain networks
    * One must be cautious when interpreting findings, as the neural origins of spontaneous signals are not well understood and the fMRI signal is susceptible to noise
* **Target audience**: Faculty and trainees interested in fMRI methodology, specifically resting-state functional connectivity.
* **Purpose:** To introduce the concept of task-free fMRI and describe characteristics of spontaneous BOLD signal fluctuations, surveying current evidence and theories regarding their origins and relevance. Material in this lecture will also serve as background information for subsequent talks in the session.
* **Outcome/Objectives:** To obtain a basic understanding of spontaneous BOLD fluctuations and functional connectivity.

Functional MRI experiments have traditionally focused on brain activity evoked by external stimuli or task demands, while disregarding task-unrelated ("intrinsic" / "ongoing" / "spontaneous") fluctuations. Interest in spontaneous fluctuations was kindled by the study of Biswal et al., who showed that regions activated in a sensorimotor task exhibited spatially specific, temporally correlated BOLD signal fluctuations in a resting-state scan [1]. Subsequent work revealed that spontaneous fluctuations across the brain exhibit remarkable spatio-temporal structure and consistency ("resting-state networks"), aligning with known functional systems. Examining the co-variation of BOLD signal fluctuations in task-free fMRI scans has been widely used for interrogating networks within and across individuals and populations.

Yet, much remains to be understood concerning the neural origins and relevance of spontaneous BOLD fluctuations and correlations (see, e.g., [2,3] for reviews). We will discuss characteristics of these fluctuations and their relationship to electrophysiological measures, structural connectivity, task activation, and behavior. For example, some degree of correspondence has been obtained between spontaneous BOLD signals and fluctuations in the power of EEG and local field potentials at certain frequency bands. Resting-state networks resemble, though tend to extend beyond, direct structural connections, suggesting that direct anatomical connections shape (but do not fully constrain) the strength and topology of correlated fluctuations; factors such as synaptic efficiency and myelination also likely contribute. The behavioral relevance of spontaneous BOLD fluctuations has been demonstrated through studies showing, for instance, that pre-stimulus levels of intrinsic activity can significantly predict task responses.

Beyond the challenges of understanding the origins of spontaneous activity, inferences made from the resting-state BOLD signal are confounded by the contribution of non-neural "noise" to the measured fMRI signal, such as due to respiratory/cardiac processes and head motion. Moreover, in the absence of a task, the distinction between signal and noise in resting-state data cannot be informed by *a priori* models of neural activity, and therefore employing noise reduction strategies is critical.

References: [1] Biswal, B. et al., 1995. Functional connectivity in the motor cortex of resting human brain using echo-planar MRIMagn Reson Med 34, 537-541. [2] Leopold, D.A., Maier, A., 2012. Ongoing physiological processes in the cerebral cortex. Neuroimage 62, 2190-2200. [3] Buckner, R.L., 2010. Human functional connectivity: new tools, unresolved questions. PNAS 107, 10769-10770.