Curso C

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Parameter estimation unidentifiability in models and degeneracy in biological systems: two faces of the same coin

The interpretation of experimental and observational data is typically based on mathematical models whose goals are to describe these data, make predictions, or explain the mechanisms that give rise to the data in terms of the interactions of the system's components. Whether the models are primarily statistical or dynamic, they involve parameters that need to be fit to data coming from experiments or observations. The ability of the models to make predictions and to provide mechanistic explanations depends on the accuracy and reliability of this process. A key feature of parameter estimation tools is the minimization of the error (using the appropriate metrics) between the model output (simulation using estimated parameters) and the available data. There are several difficulties associated with the implementation of these tools. These difficulties are technical (algorithmic nature), statistical (data is noisy and therefore one can at best expect to estimate distributions of parameter values around a "true" mean), and structural (degeneracy, mathematical nature). Degeneracy refers to these situations where multiple sets of parameter values can produce the same observable output (e.g., evolution curve in an epidemic model, oscillatory patterns in a biological clock), therefore making the inverse problem (of finding parameters given the data) ill posed. This type of unidentifiability is not a problem associated with the statistical uncertainty in the knowledge of a unique parameter set from which the data is generated referred to above, but a structural problem inherent to mathematical models where the same patterns (e.g., temporal, spatial) can be obtained from multiple parameter sets. Moreover, this type of degeneracy has been observed in biological experiments and is expected to be pervasive. In this short course we will discuss these issues in the context of biological oscillations using a number of representative models both biologically realistic (e.g., describing oscillations in individual neurons and neuronal networks) and caricature (toy) models. The latter are particularly useful to link the phenomena of unidentifiability/degeneracy to the symmetries present in dynamical systems.