

Exploring Time-Series Phosphoproteomic Datasets in the Context of Network Models

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Abstract : Time-series data are useful for modelling as they can enable model-evaluation. However, when reconstructing models from phosphoproteomic data, often non-exact methods are utilised, as the knowledge regarding the network structure, such as, which kinases and phosphatases lead to the observed phosphorylation state, is incomplete. Thus, such reactions are often hypothesised, which gives rise to uncertainty. Here, we propose a framework, implemented via a web-based tool (as an extension to Minardo), which given time-series phosphoproteomic datasets, can generate κ models. The incompleteness and uncertainty in the generated model and reactions are clearly presented to the user via the visual method. Furthermore, we demonstrate, via a toy EGF signalling model, the use of algorithmic verification to verify κ models. Manually formulated requirements were evaluated with regards to the model, leading to the highlighting of the nodes causing unsatisfiability (i.e. error causing nodes). We aim to integrate such methods into our web-based tool and demonstrate how the identified erroneous nodes can be presented to the user via the visual method. Thus, in this research we present a framework, to enable a user to explore phosphorylation proteomic time-series data in the context of models. The observer can visualise which reactions in the model are highly uncertain, and which nodes cause incorrect simulation outputs. A tool such as this enables an end-user to determine the empirical analysis to perform, to reduce uncertainty in the presented model - thus enabling a better understanding of the underlying system.

Keywords : κ -models, model verification, time-series phosphoproteomic datasets, uncertainty and error visualisation

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