Sharing comprehensible physiological models
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Background
As our knowledge of physiological systems increases, computational models developed to help explore and understand these systems are becoming better approximations of the real world. Inevitably this leads to more complex models which are difficult to share with colleagues in a useful manner. Efforts such as the IUPS Physiome Project, Virtual Physiological Human, and Virtual Physiological Rat help to push the boundaries of computational physiology to enable the kind of multiscale modelling illustrated here.

As biosimulation models increase in size and complexity, it becomes impossible to reuse a given model from the primary publication of the model in traditional scientific literature alone. This issue is further complicated by the need to dive deeper into a biosimulation model’s description in order to gain insight into its suitability for a given scenario. The source of model parameters, for example, is often hard to discover – exemplified by the study from Niederer et al shown to the left.

As the biosimulation models move toward clinical application, more complications arise interpreting both the models and their predictions. The example on the left from Mirams et al demonstrates the need to describe the uncertainty and variability.

Methods
The adoption of standards to encode mathematical models and simulation experiments allows scientists to leverage existing domain specific tools to explore and interact with the models and simulation experiments, as illustrated below.

Enhancing the encoded biosimulation models with computable descriptions of their provenance, construction, limitation, validation, etc, information further improves their discoverability and understandability.

Repositories such as the Physiome Model Repository (PMR; https://models.physiomeproject.org/) are then able to provide discovery and comprehension services using this knowledge.

Here we show examples of the types of information and knowledge available in the Physiome Model Repository. Above is the Noble 1962 model with Mathematica, generated code, and “launched in OpenCOR”. To the left, an example FieldML model and a synthetic biology example.

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Results
We are beginning to build tools which make use of these semantic-web based discovery and comprehension services. The example below illustrates a model discovery and assembly tool that is being developed by Dewan Sarwar at the Auckland Bioengineering Institute.

The example above demonstrates the points of biological similarity for two entities from different CellML models.

As tools such as these evolve, we hope to demonstrate the added value to scientists putting in the extra work to make their models available as described here. To this end, the IUPS is launching a new “journal” to be called Physiome, which will provide a mechanism to publish curated and annotated models and track their reuse by the scientific community. See journal.physiomeproject.org for more information.

Standards are being developed to address the need to enable biosimulation models to be shared in a reproducible and reusable manner. The Computational Modelling in Biology Network (COMBINE) is an effort to coordinate the development of such standards.

http://co.mbine.org/

https://dx.doi.org/10.1113/expphysiol.2008.044610

https://dx.doi.org/10.1113/JP271671

http://combine.org/