Towards multiscale modelling in Systems Biology

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Overview

• Computational modelling & analysis of biochemical networks:
  – *Explain* behaviours and mechanisms
  – *Predict* behaviour of a system under different conditions.

• Represent biological systems as networks often containing regular structures, i.e. *repeated occurrences of network patterns*.

• *Hierarchical organisation* reflecting physical & spatial organisation of the organism, intracellular to the intercellular level and beyond (tissues, organs etc.).

• *Multiscale modeling*: solving physical problems which have important features at multiple scales, particularly multiple spatial and/or temporal.

• *Focus on spatial aspects* – multiscale time comes ‘for free’.

• Current modelling approaches, including Petri nets: limited to relatively small networks.

• *Hierarchy + colour* in Petri nets: supports modelling of large and complex biological systems.
BioModel Engineering

• Takes place at the interface of computing science, mathematics, engineering and biology.

• A systematic approach for designing, constructing and analyzing computational models of biological systems.

• Some inspiration from efficient software engineering strategies.

• Not engineering biological systems per se, but
  – describes their structure and behaviour,
  – in particular at the level of intracellular molecular processes,
  – using computational tools and techniques in a principled way.


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Multiscale challenges
What about scaling up?
Multiscale modelling challenges

- **Repetition** – multiple components with similar definitions
- **Variation** – genetic mutants; random variants
- **Spatial organisation** - regular / irregular patterns in 1, 2 or 3 dimensions
- **Communication** – short & long distance
- **Hierarchical organisation** – intra or inter cellular (tissues, organs, …)
- **Movement** – mobility (passive) & motility (active)
- **Replication** - reproduction
- **Exchange** of genetic information
- **Death** – apoptosis, necrosis, etc (quiescence, senescence)
Repetition of individual components

- Components within a cell (organelles etc)
- Multiple cells each of which having a similar definition
- Repeated tissue fragments
- Repeated organs (wings, …)
- Repeated individual organisms
Variation

- Sets of similar components with defined variations
- Random mutation
- Genetic mutants
- Cancerous tissue
- Differentiation

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Multiscale challenges
Spatial organisation

• Between cells
  – how they are organised into regular or irregular patterns over spatial networks in one, two or three dimensions.
Communication

- Between **immediate neighbours** (intracellular complexes)
- **Long-distance** (cytokines etc)

Further constraints:
- Type of **relationship** between partners
- Type of component(s)
- History of component(s)
- **Position** of component(s) in spatial network.

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Multiscale challenges
Hierarchical organisation

Components containing repeated sub-components

• Cell containing several compartments /components.

Enables the use of abstraction over level of detail used to describe components
Movement

- Mobility – passive movement.
  - Protein transport
  - Sodium transport

- Motility – active movement.
  - Cells using organelles (flagellae)

General cellular motility
Replication

- E.g. cell division

Can take into account:
- Mutation
- Spatial organisation / position
Exchange

• Exchange of (genetic) information
• Sexual
• Asexual
Death etc

- Cell death:
  - apoptosis (programmed), necrosis (traumatic)
- Quiescence
- Senility
Modelling challenges

How to:

• Design & construct models
• Simulate models
• Visualise results
• Check models
• Analyse models
• Validate models
Day 2: Multiscale Systems Biology

8.30 – 9.00: Welcome Coffee

9.00 – 11.10:

BioModel Engineering via modular, protein-oriented modeling [Mary Ann Blätke]

Introduction: Moving to the multiscale in systems biology modeling. [David Gilbert]

Advanced modeling concepts:

- Coloured, and hierarchically coloured Petri nets + Exercise [Monika Heiner]

Detailed discussion and analysis of examples:

- *C. elegans and calcium channels* [Fei Liu]

11.10 – 11.40: Coffee Break

11.40 – 13.30:

Detailed discussion and analysis of examples:

- *Halobacterium salinarum* [Wolfgang Marwan]

- *Drosophila melanogaster* - planar cell polarity in tissues [Qian Gao, Esther Bamigboye]

Analysis techniques for multiscale models [Mary Ann Blätke, Daniele Maccagnola]

Discussion: Challenges in multi-scale modeling for systems biology

13.30 – 14.00: Lunch
Some references


