Multiscale Systems Biology

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Multiscale – really?

What do we mean by

*Multidimensional*

*Multiscale*

*Multilevel*
Scaling up?
... scaling down???

**QUATERNARY STRUCTURE**

**PRIMARY STRUCTURE (amino acid sequence)**

VHLTI
VGGE
SFGD
KKVL
TLSEI
VLVC
QKVV

**SECONDARY STRUCTURE (helices, strands)**

**TERTIARY STRUCTURE (fold)**
Multiscale Modelling in Biology

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Multiscale Modelling Challenges

• **Repetition** – multiple components with similar definitions
• **Variation** – genetic mutants; random variants
• **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) (Components could be molecules, organelles, cells, tissues, organs, organisms.)
…Multiscale Modelling Challenges

• **Replication** - reproduction
• **Deletion** – cell death
• **Irregular/semi-regular organisation** of components – for example a not-exact honeycomb grid.
• **Dynamic grid size** – for example alter size and/or topology of grid to model development. Also required for ability to insert/remove items.
• **Differentiation of components** - for example, differentiation of embryonic stem cells or immune cells makes a less specialized cell more specialized.
• **Pattern formation of components** - organizing a number of cells in appropriate one, two or three dimensional structures in space and time.
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
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.
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
Replication

E.g. cell division

Can take into account:
• Mutation
• Spatial organisation / position
Exchange of (genetic) information

- Sexual
- Asexual
Death etc

- Cell death: apoptosis (programmed), necrosis (traumatic)
- Quiescence
- Senility
Life – patterns: beauty...
Concepts

• Multiple scales: time; space (1, 2, 3D),
• Development
• Hierarchy of organisation in organisms
• Levels in hierarchy: inherently associated with t, s scales?
• Atomic, molecular, sub/intracellular (organelles, compartments), cellular, intracellular, tissues, organs,…
• Hierarchy – tree (partially ordered upper semi-lattice).
Levels, Hierarchy

Level n+1

T

Level n
And then…

How do we CHECK that the models are ‘correct’?
Newton Advanced Fellowships
Royal Society &
National Natural Science Foundation China

- [closed]

- Applicants must have a PhD or equivalent research experience and hold a permanent or fixed-term contract in an eligible university or research institute, which must span the duration of the project. Applicants should have no more than 15 years of postdoctoral experience. Collaborations should focus on a single project involving overseas-based scientist (“the Applicant”) and UK-based scientist (“the Co-applicant”).
Research Councils UK - China

- [http://www.rcuk.ac.uk/international/Offices/china/](http://www.rcuk.ac.uk/international/Offices/china/)
- Very specific schemes
- Overview of China for non-Chinese:
  - [http://www.rcuk.ac.uk/international/offices/china/research-landscape-in-china/](http://www.rcuk.ac.uk/international/offices/china/research-landscape-in-china/)