A Multi-Scale Model of Saliva Secretion

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Salivary glands
• Three types: serous, mucous and mixed
• $Ca^{2+}$ increases the open probability of the $K^+$ and $Cl^-$ channels
• An ionic gradient is established which allows water to flow to the lumen by osmosis
Real-world experiment data

A

B

C

D. Yule
Modelling calcium response

“Calcium waves”
Synthetic modelling
FEM meshes
Synthetic model: saliva production

Intracellular in mM (Cell #1)

- Na
  - 13.27
  - 12.36
  - 11.46

- K
  - 147.68
  - 146.51
  - 145.34

- Cl
  - 60.06
  - 56.03
  - 51.99

Time t = 23.01 in s

Flow in um/s

Conc in mM

Duct distance from Lumen in um

Time T in secs
Why a multi-scale model?

● Why multi-scale? Because events at the molecular level within cells can directly influence saliva secretion at the level of the entire organ.

● Why modelling? There are many questions that are difficult to answer experimentally but that can be addressed with a quantitative model.

● Our goal, using both modelling and experiment, is to understand how changes at the level of individual molecules and channels will affect organ-level behaviour.

● In other words, our goal is the study of interactions. Of course, our model is still preliminary and incomplete. It's also mostly unpublished…
Modelling hierarchy

Physical scaling

Cells
Tissue
Organs

Same for computational scaling!

One
More
Many
NeSI Project plan (technical)

- Port existing development code to the cluster
- Create progressively more realistic 3D synthetic meshes
- Create fully realistic 3D meshes from digitisations
- Re-implement and parallelise the development code
- Scale-up the code to larger models (more cells!)
- Re-use realistic 3D meshes for visualising simulation results
- Verify simulated results with real-world measurements
Abitrary synthetic mesh creation

Cell mesh
Arbitrary synthetic mesh creation

Embedded structure
Abitrary synthetic mesh creation
Cut-away view
Arbitrary synthetic mesh creation

Cut-away view
Confocal microscopy: image stacks

Approximately 150um square

- Fluorescent markers target different proteins in the same sample
- Precisely aligned image acquisition!

D. Yule
Confocal microscopy: image stacks

Approximately 70um square

- Fluorescent markers target different proteins in the same sample
- Precisely aligned image acquisition!

Cells
Lumen

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Real-world geometry
3D reconstruction

Approximately 150um square
3D reconstruction: cells and lumen

Approximately 70um square
3D reconstruction: cells and lumen

Approximately 70um square
Project status

• Just finished three month NeSI Proposal development stage

• NeSI Research Project application submitted in May

• Next (technical) step: Run development code on progressively more realistic meshes

More to come…