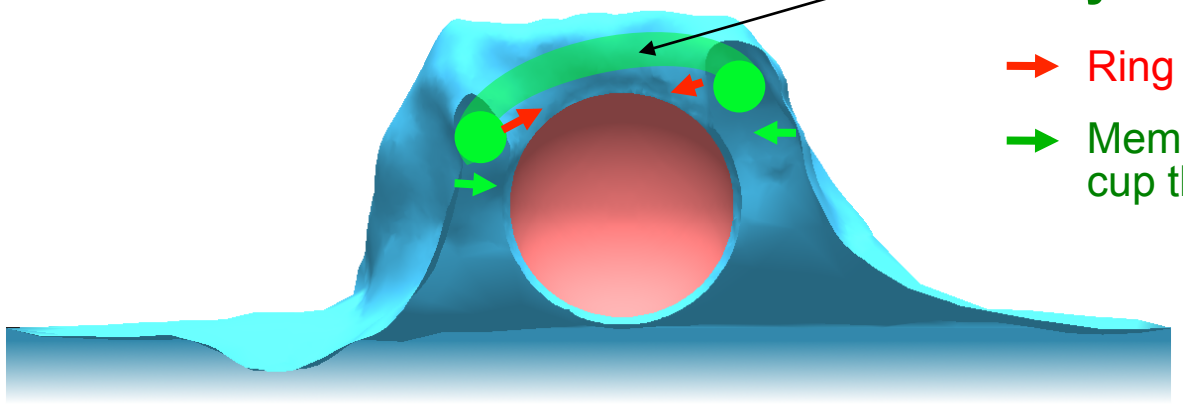
New model to explain experimental data

Reconcile the end of engulfment with experimental observations

Previous discrepancy indicates predominance of contractile forces

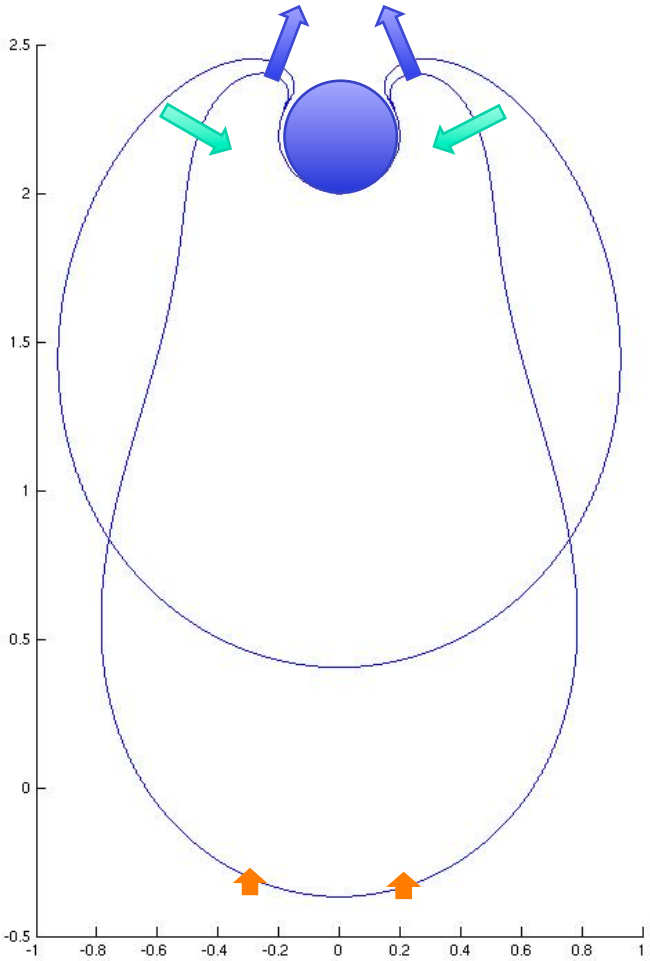
Contractile forces = actin cytoskeleton + myosins



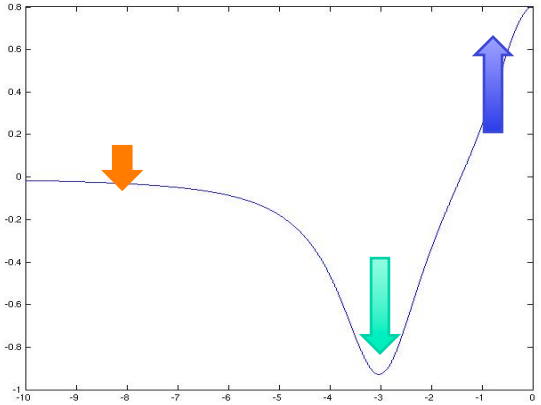
- Ring contraction accelerates cup closure
- Membrane-Ring contraction makes closing cup thinner

Finding the membrane equilibrium shape

Preliminary result: cell shape for given applied pressure profile



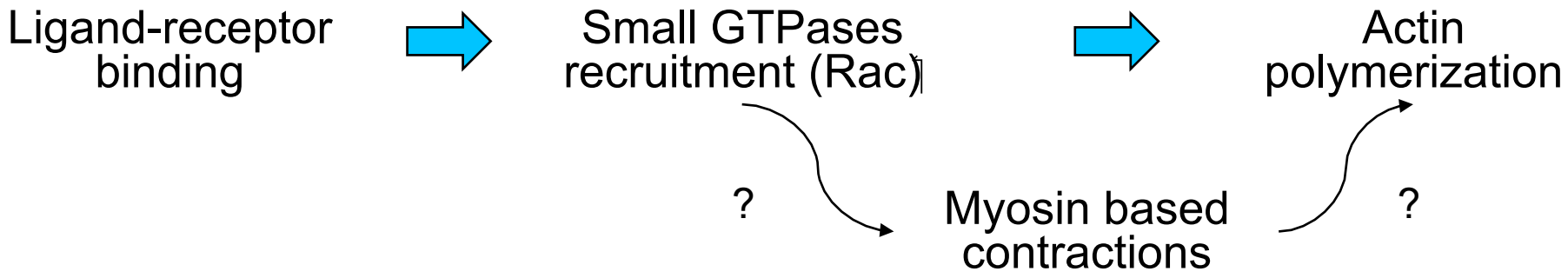
Applied pressure profile (force on membrane):



Derive pressure profile from model for cytoskeleton and signalling

A continuous model for cell processes

Signaling pathway



Model philosophy

Model ingredients

- Self-activated Rac stimulates actin polymerization (actin waves)
- Polymerized actin inhibits Rac production
- Cytoskeleton isotropic contraction due to bulk myosins
- Membrane/cytoskeleton contraction due to surface myosins

Model flexibility: interaction with experiments

Method and first results

System's evolution: PDEs, discretization, boundary conditions

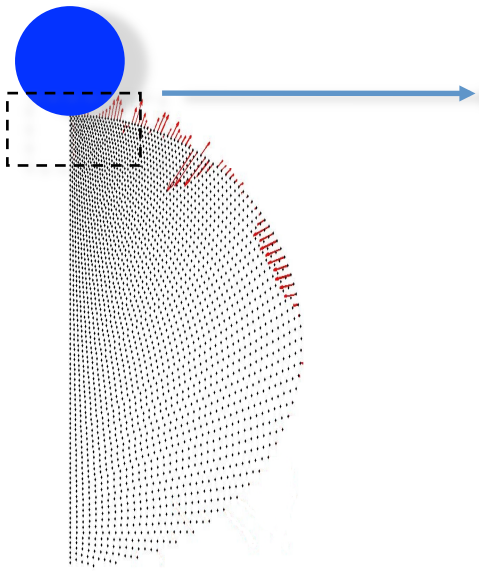
Given membrane shape:
boundary conditions (BC)
for PDE system

Solve PDEs
with given BC
t → t+dt

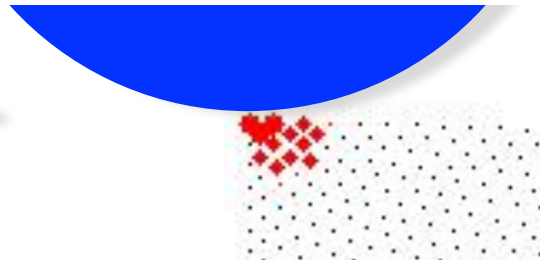
Solve for
membrane
shape
at time t+dt

Calculate force distribution
on outer membrane

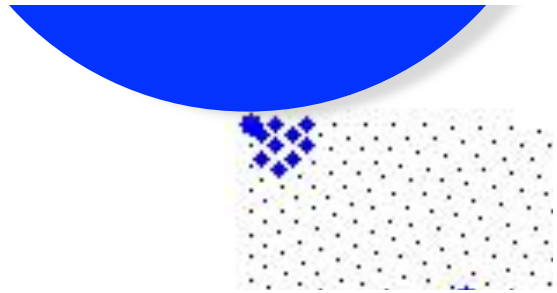
Mesh & surface forces



Actin network



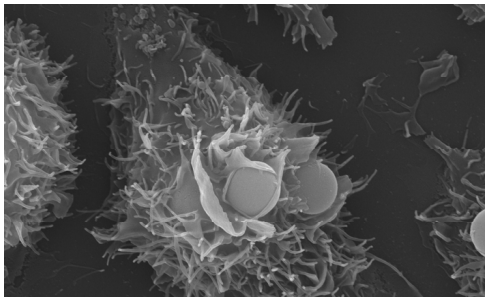
Signaling molecule



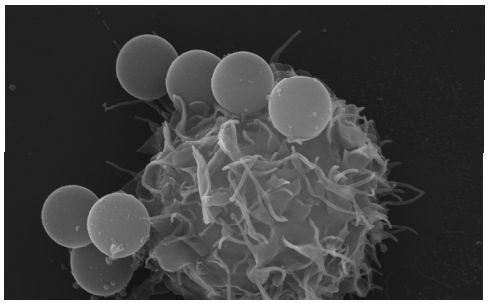
Non uniform mesh for
optimal computations

Experiments to inform and validate model

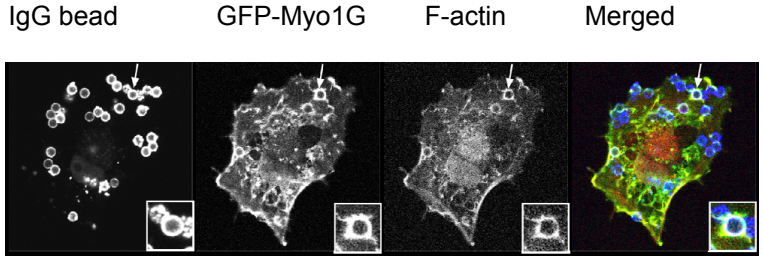
Myosin 1G is involved in phagocytic engulfment



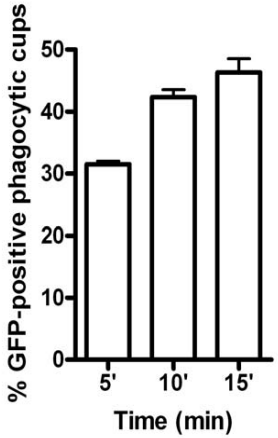
Wild-type J774A.1 macrophages (no treatment)



ML-7 treatment (Myosin light-chain kinase inhibitor)

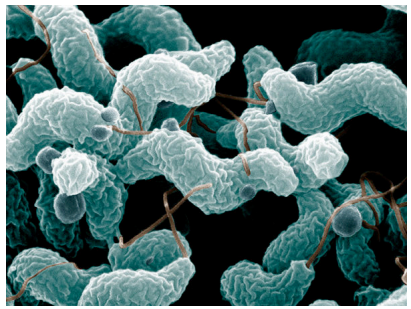


Myo1G recruited to cups



Future plans

- Investigate other myosin isoforms and conduct RNAi knockdowns
- With **Subproject 1**: use spiral-shaped *Campylobacter* for phagocytosis assays



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- Gadi Frankel
- Brian Robertson
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- Sally-Ann Cryan (Dublin)

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- Suhail Islam
- Martin Spitaler
- Chris Tomlinson

Facility for Imaging by Light Microscopy
FILM
Observing Life As It Happens

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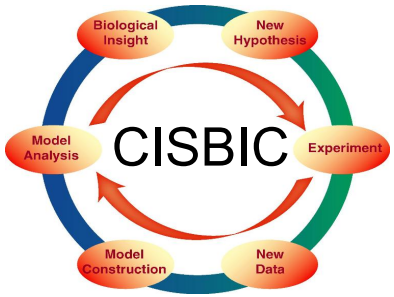

BBSRC
bioscience for the future

- Current Grant BB/G000131/1
- Submitted BBSRC Grant application to continue work with co-investigators Brian Robertson and Gadi Frankel