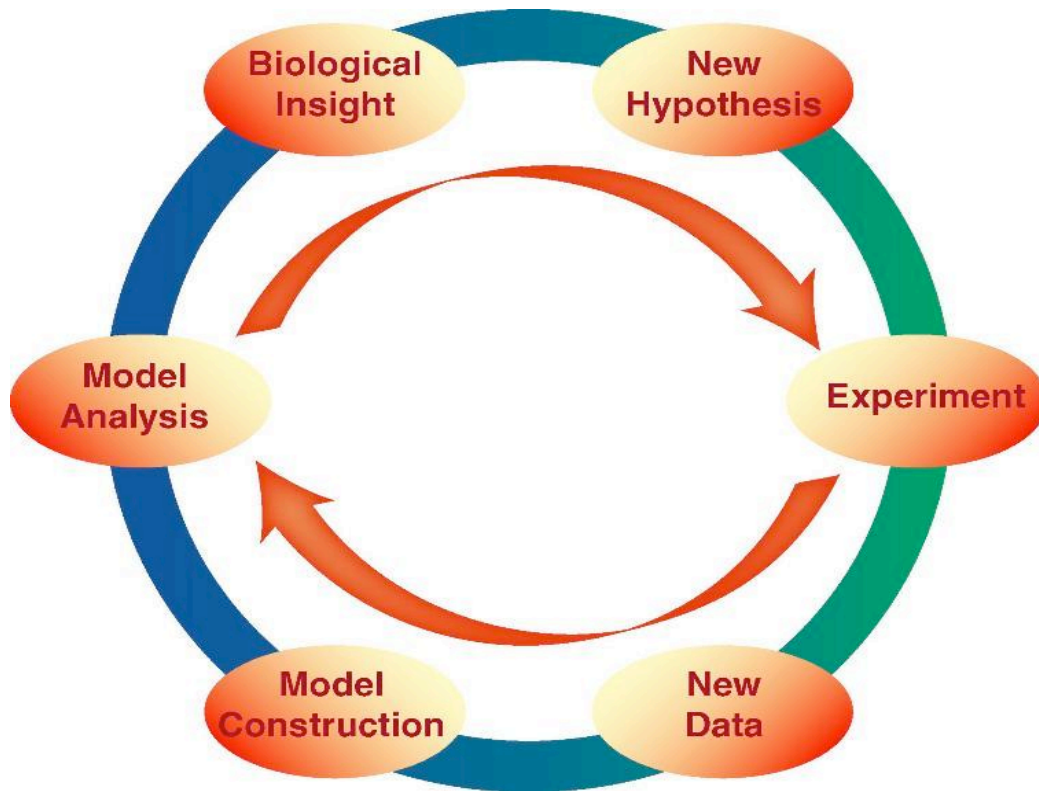


02-03-2008

CISBIC subproject meeting

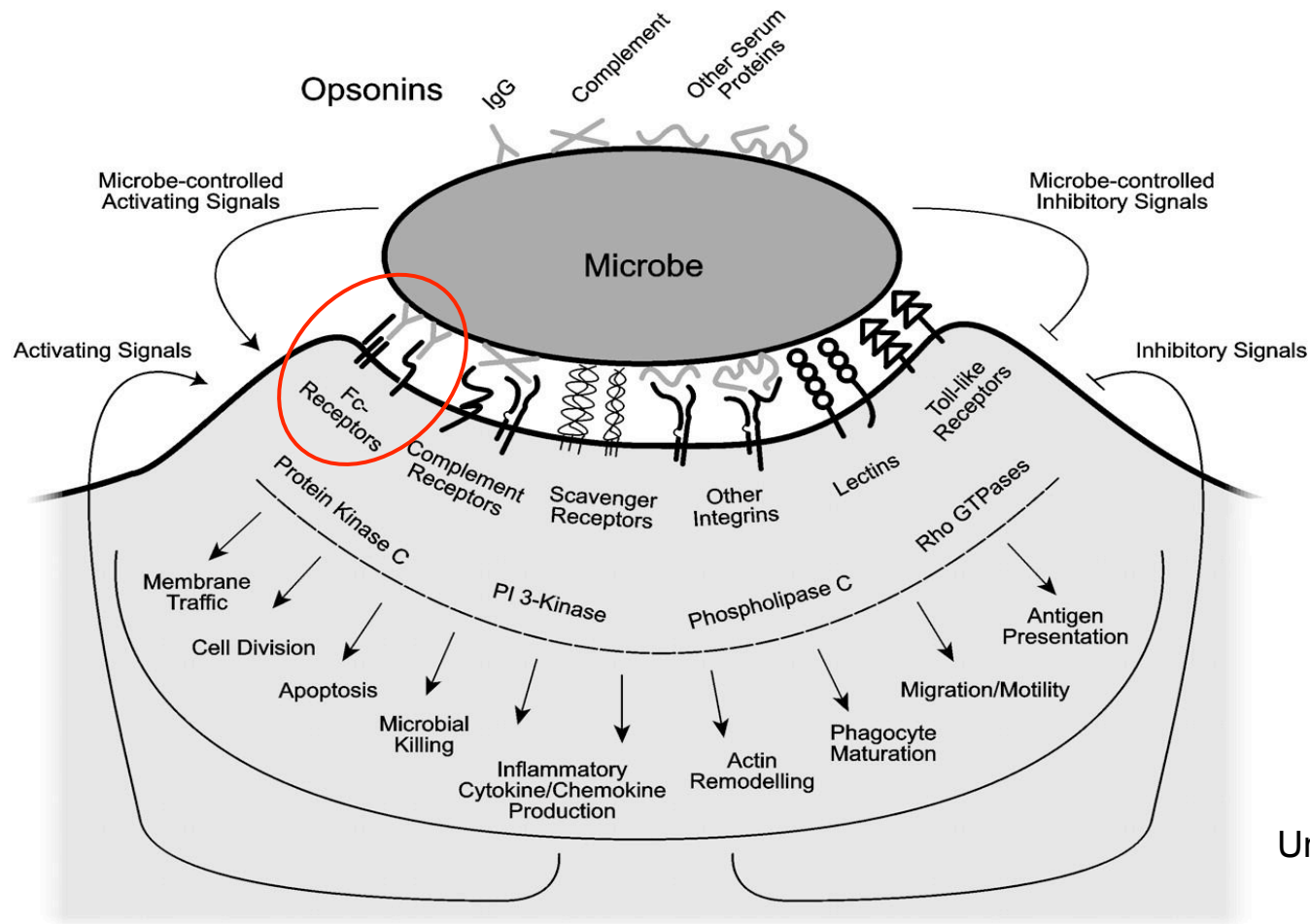
Sub-project 2



Understanding phagocytic  
receptor localisation and  
signalling

George Tzircotis

# Analysis of early signaling following phagocytic receptor engagement



## Aims - Biological sub-project 2

Experimental work divided into two parts:

- A - Fc receptor dynamics during early stages of phagocytosis -  
(with Jeroen Van Zon / Martin Howard)
  
- B - Identification of molecules involved in phagocytosis signalling networks

## Aims - Biological sub-project 2

A - Fc receptor dynamics during early stages of phagocytosis -  
(with Jeroen Van Zon / Martin Howard)

Generation of Fc receptor mutants (GT)

Confocal microscopy of live/fixed cells undergoing phagocytosis  
under various conditions (GT)

Generation of model for Fc receptor distribution (JVZ/MH)

## A. Fc receptor dynamics during early stages of phagocytosis

Experimental work -

Use of confocal microscopy to analyse:

Diffusion of receptors across membrane

Movement of Fc receptors in and around phagocytic cups during phagocytosis (time-courses) -

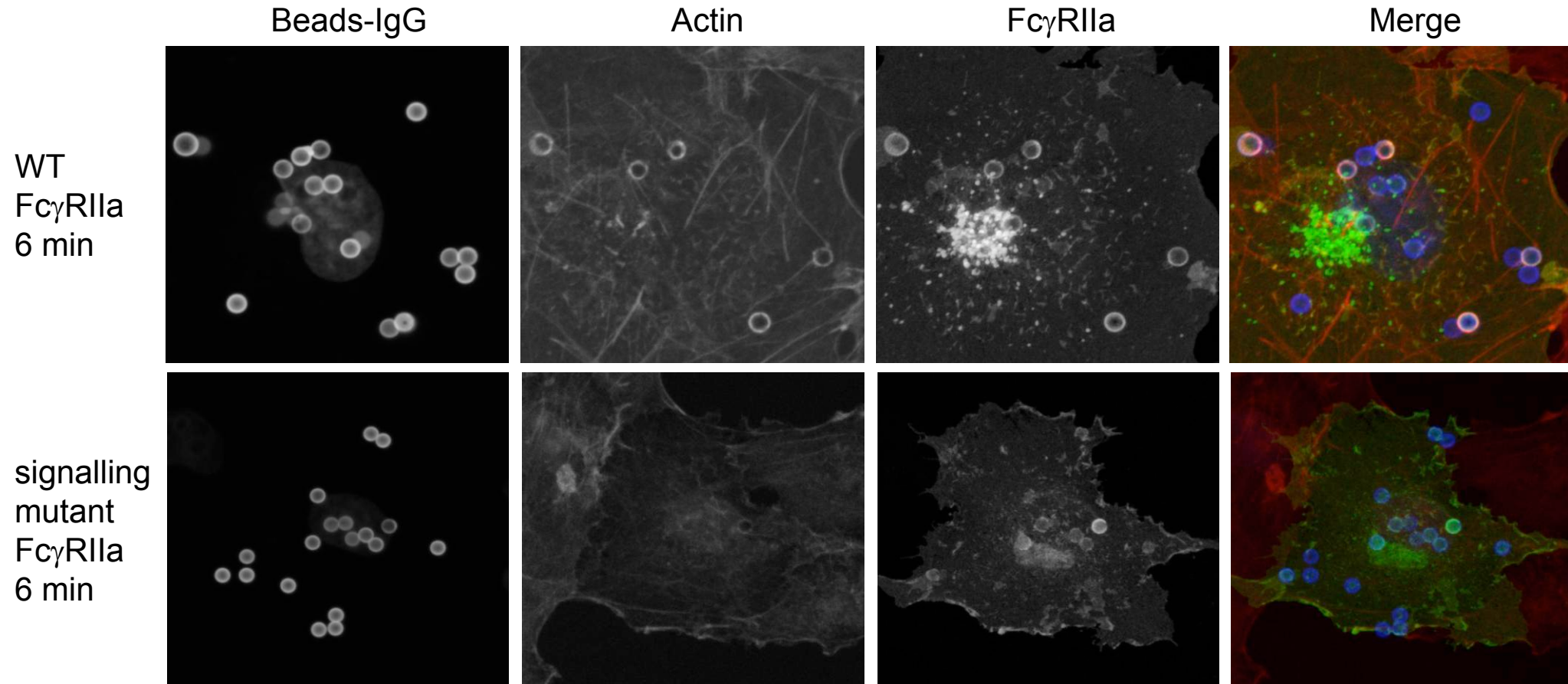
done for a variety of mutants:

wild type, signalling mutant, deleted cytoplasmic tail...

and particle sizes

# A. Fc receptor dynamics during early stages of phagocytosis

## Example images



## A. Fc receptor dynamics during early stages of phagocytosis

### Observations:

Fc receptor (but not actin) cups are still able to form in mutants:

- medium particles have uneven/misshapen Fc receptor cups
- small particle mutant Fc receptor cups look similar to wild type

Very large particles begin to form cups but do not progress

Collected time-course data for Fc receptor and actin localisation

# A. Fc receptor dynamics during early stages of phagocytosis - Modelling

## Membrane shape model

Constructed model coupling membrane/cytoskeletal dynamics to receptor diffusion and signalling

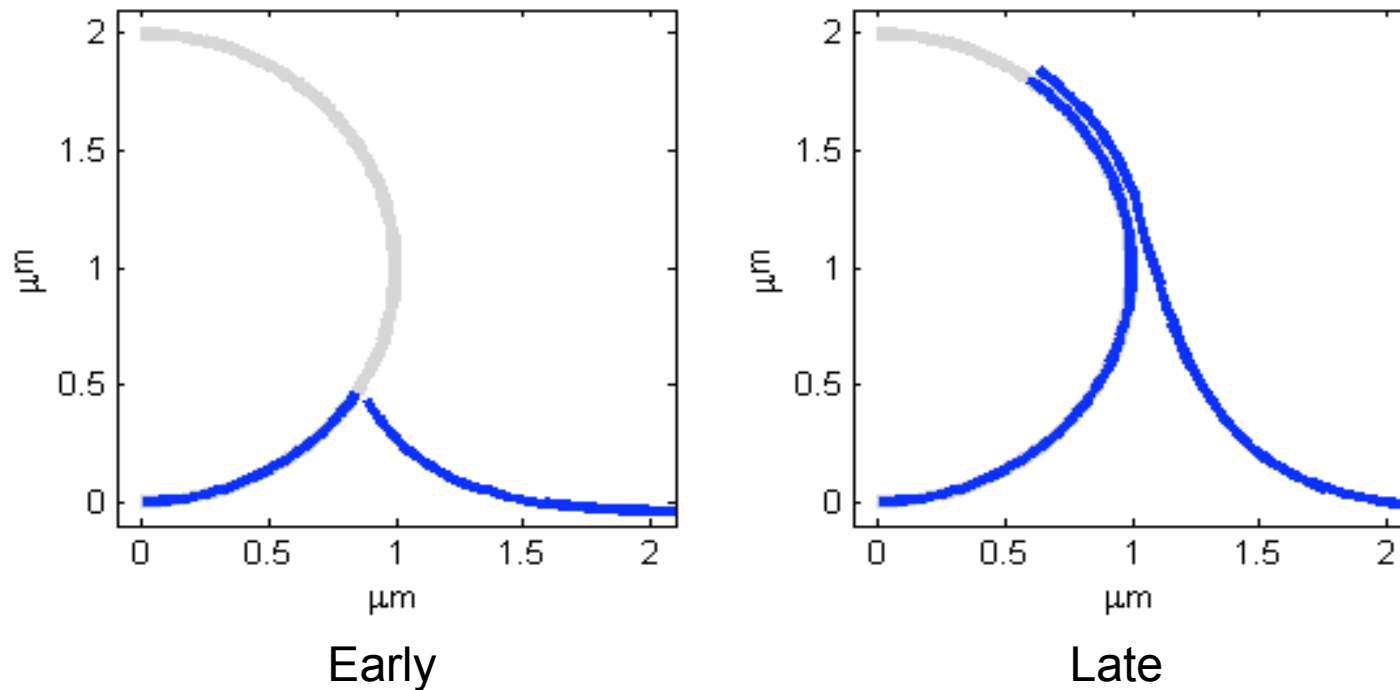
Completely determined by **bending modulus** and **cortical tension**

Model correctly predicts shape of cup



# A. Fc receptor dynamics during early stages of phagocytosis - Modelling

Phagocytic cup shapes predicted by membrane model



Force required to make a cup of certain size can be calculated

# A. Fc receptor dynamics during early stages of phagocytosis - Modelling

Diffusion model

QuickTime™ and a  
Animation decompressor  
are needed to see this picture.

Fc receptors bind antibody on particle and stimulate actin polymerisation

Local actin polymerisation provides force for cup formation

## A. Fc receptor dynamics during early stages of phagocytosis

### - Future plans

- Further analysis of microscopy data, spatio-temporal localisation of Fc receptor and actin. Add to model
- Incorporate more complicated signalling dynamics, get more realistic results