Brief introduction to cell polarity. Make the point that this is underlied by the asymmetric localisation of polarity proteins on their membranes. It is these proteins that define an initial asymmetry in cells, and drive an array of downstream processes to carry out the functional roles of polarity

Cell polarity describes any phenomenon whereby biochemically distinct regions are set up in a cell. This feature is remarkably common and serves a number of purposes.

**SPATIAL PATTERNING IN BIOLOGICAL SYSTEMS**

*A general overview of the mechanisms that can contribute to pattern formation in biological systems, with a particular focus on mechanisms of relevance to this work*

**Reaction-diffusion models**

* *Key concepts: mass action kinetics, local activation/long-range inhibition, Turing patterns, pattern triggering*

Figure: formation of 2D Turing pattern

* E.g. http://www.scholarpedia.org/article/Gierer-Meinhardt\_model
* Patterning by directed transport

**CELL POLARITY**

See notes

Figure: examples of cell polarity

**The Min system**

**CDC-42 polarity in yeast**

**PAR polarity**

Figure: PAR polarity in the C elegans zygote

* See RI 1.7

**MAINTENANCE OF CELL POLARITY BY BISTABLE REACTION-DIFFUSION SYSTEMS**

*A review of bistable polarity models, and a discussion of their mathematical requirements*

**Bistable reaction kinetics**

*Introduce the concept of bistability, the need for non-linear (ultrasensitive) reactions, relate to pattern formation*

**Single species polarity models**

*Demonstrate key concepts: local amplification, pool depletion, parameter space topology, using examples (WP, GOR, OT)*

*Requirements for non-linear feedback*

**The mutual antagonism model**

*Link to single species models: parameter space topology, local amplification, pool depletion, requirements for non-linear feedback all equivalent*

*Summarise key parameter dependencies previously explored (e.g. requirements for balanced antagonism/dosages, diffusion rates/relation to system size)*

*Models with additional feedback reactions tend to be more robust*

**A MOLECULAR BASIS FOR ULTRASENSITIVITY**

*An overview of some molecular mechanisms that can generate ultrasensitive kinetics, with a focus on mechanisms relevant to this work*

**Ultrasensitivity in protein phosphorylation reactions**

*Multisite phosphorylation, cooperativity, requirements for ultrasensitivity*

**Ultrasensitivity from positive feedback reactions**

*Drawing a general link between positive feedback reactions and ultrasensitivity. Mathematical requirements*

**Positive feedback from cooperative membrane binding**

*Review of existing cooperative binding models, link to protein oligomerisation*

*E.g. Dawes and Munro model, and others not necessarily related to the PAR network (e.g. Sophie Martin)*

**PAR POLARITY IN C. ELEGANS**

*A detailed review of PAR polarity in C. elegans, referencing ideas raised thus far*

**The PAR proteins**

*Brief introduction to the main molecular players and their roles*

**Methods for quantitative analysis of PAR protein dynamics**

*Confocal imaging, concentration quantification. Introduce the idea of membrane affinity and membrane to cytoplasmic ratio*

*FRAP and single particle tracking (+ track analysis)*

**Mechanisms of cortical association**

*See cortical association notes*

Figure: the PAR proteins

* Schematics showing domains in all PAR proteins (like JR 1.10, 1.11)
* RI 1.10 is also good (from Lang/Munro)

**Establishment of polarity**

*See establishment notes*

**Maintenance of polarity**

*See maintenance notes*

**Antagonism resistance and substrate competition**

*See resistance notes*

**Downstream of the PAR proteins**

*See downstream notes*

**PAR-2: ROLES AND MECHANISMS OF ACTION**

*See PAR-2 notes*

Figure: RING domain dimerisation

* Example dimeric structure
* Sequence alignments for TRIM and CBL class proteins
* Table of deltaG and interface size estimates for TRIMs