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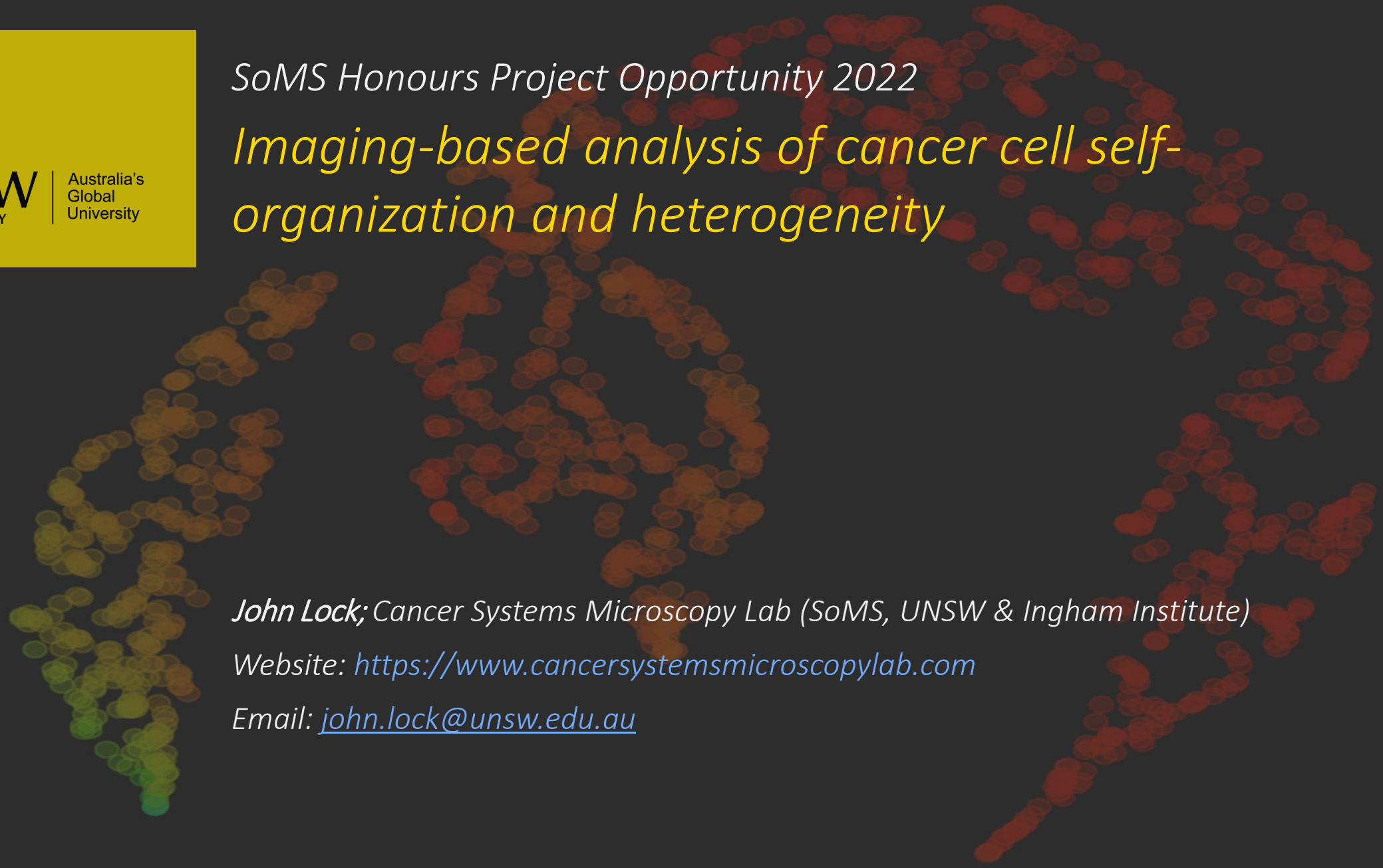
SoMS Honours Project Opportunity 2022

Imaging-based analysis of cancer cell self-organization and heterogeneity



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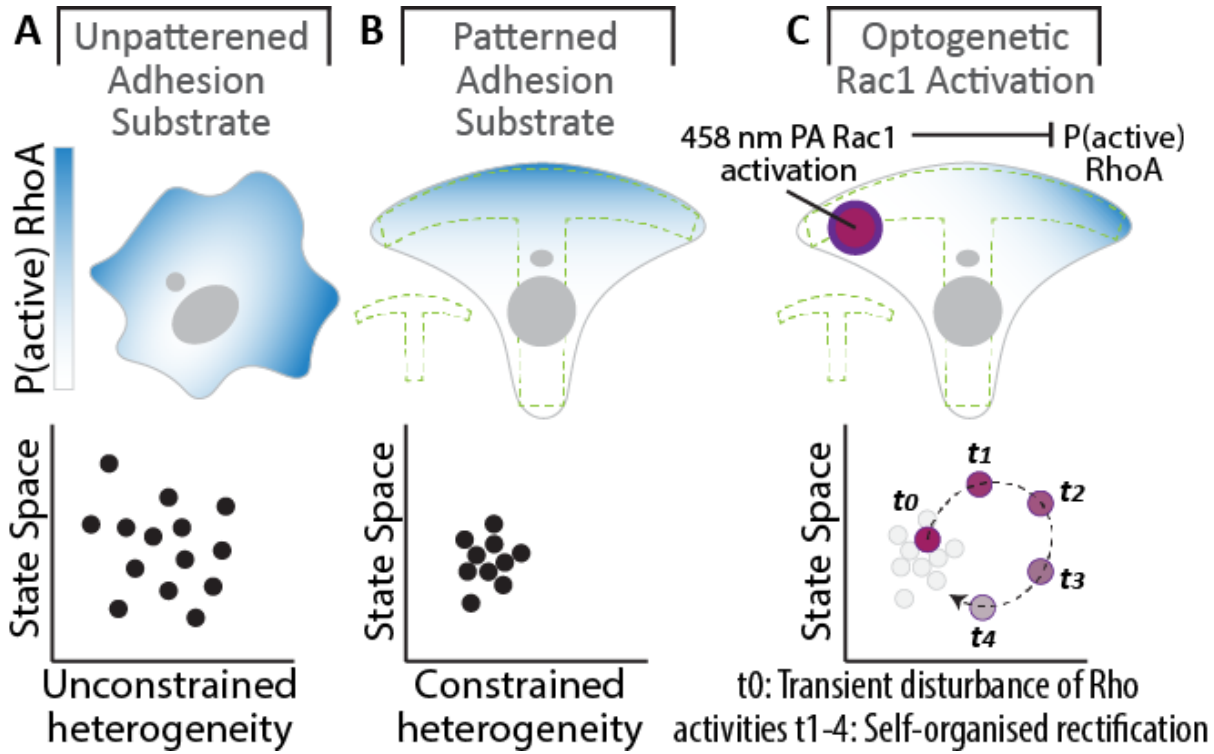
Question: *How can we study the dynamics of cellular self-organization?*

1. Cells constantly monitor diverse ‘information inputs’, i.e. exogenous chemical and physical ques
2. Given these information inputs, cells adapt their internal organization (‘state’) to compute and enact evolutionarily optimized responses
3. The process of computing and enacting responses involves cellular self-organization, which thus underpins every cellular process
4. Despite being a universal phenomena, measuring the dynamics of cellular self-organization has been difficult because information inputs are always changing, so optima are variable and always ‘moving’ (schematised in A)



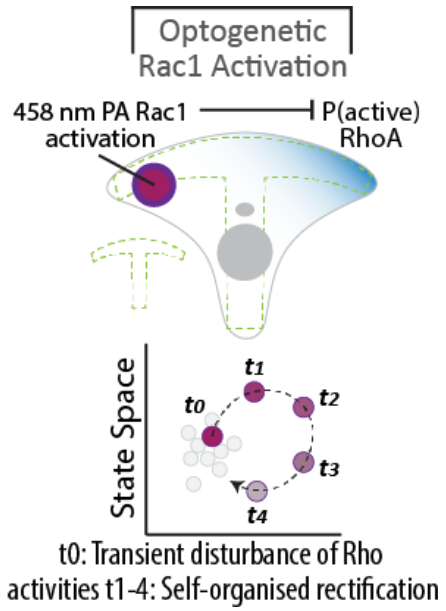
5. You will use ‘patterning’ of the cell environment to ‘lock’ information inputs, defining a stable optima (B). ‘Optogenetic’ triggers will then shift cells away from this optima, with live cell imaging monitor the dynamics of optima-return (C). This unique approach will quantify key dynamics of cellular self-organization

Our Approach: *Substrate Patterning & Optogenetics, Live Imaging Proteomic Microscopy & Machine Learning*

You will use *a world-first approach* combining substrate-patterning, optogenetics, live imaging, proteomic microscopy and machine learning to measure the dynamics of self-organisation

Cancer cells expressing optogenetic sensor & attached to controlled substrate patterns →

1. Substrate patterning, optogenetics & live cell imaging' to define optima, disrupt optima, and monito optima-return



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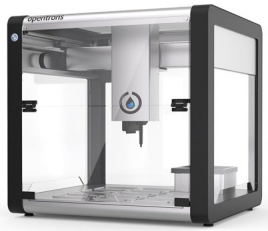
2. 'Proteomic Microscopy' involves sequential cycles of molecular labelling & imaging to detect multiplexed distributions of regulators controlling the optogenetic signalling system (Rac1)

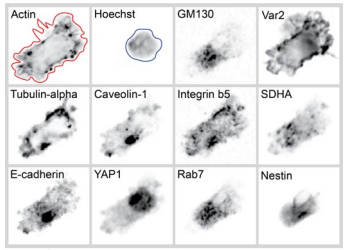
2a. Patterned Cells

2b. Automated Molecular Labelling with Liquid Handling Robotics



2c. Automated Imaging with Confocal Microscopy

2d. Multiplexed Labelling



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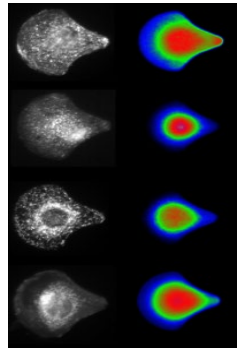
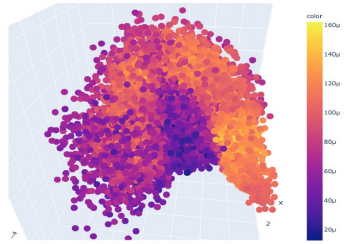
3. 'Machine Learning' for cell detection, self-organizing dynamics measurement in high-dimensional 'state' space and detection of drivers of difference. VR analytics support data analysis

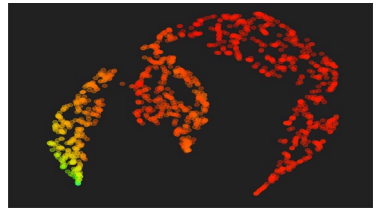
3a. Image Analysis



3b. Dynamics mapping via Deep Learning variational autoencoder & Pseudotime



3c. VR analytics & Data Visualisation



Your Role: *Tune the project to focus on your strongest interests*

- The Cancer Systems Microscopy lab uses advanced automated imaging and labelling of live and fixed cancer cell models **(1)**
- We develop and use automated image analysis and statistical analysis methods to extract insights from image data spanning 1000s of cells **(2)**
- We also develop and use machine learning and AI tools to link quantitative data analyses to immersive virtual reality data visualisation systems to improve understanding of complex data **(3)**
- You can focus across all or some of these areas, depending on what you are most excited about.