Blood, Brains, and Biofilms: Investigations of Molecular Communication in Biology

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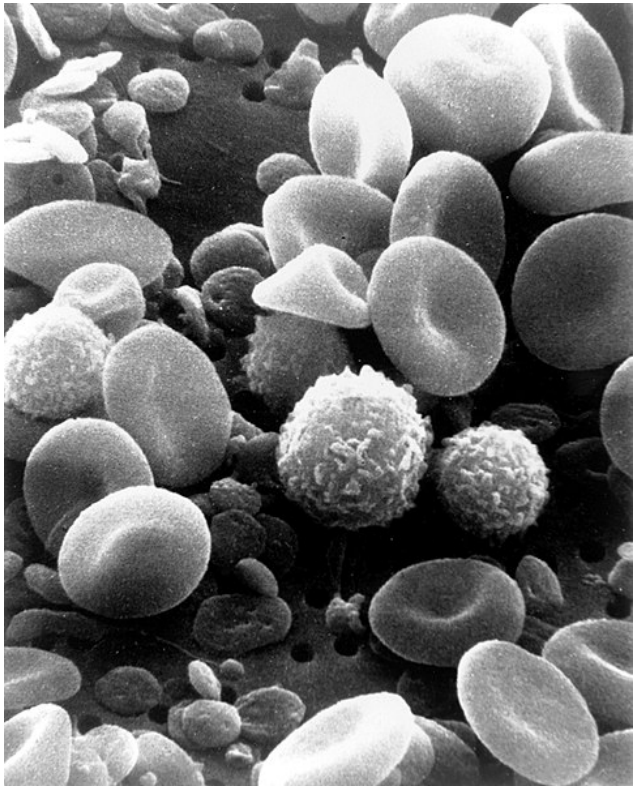
Biological Communication Networks

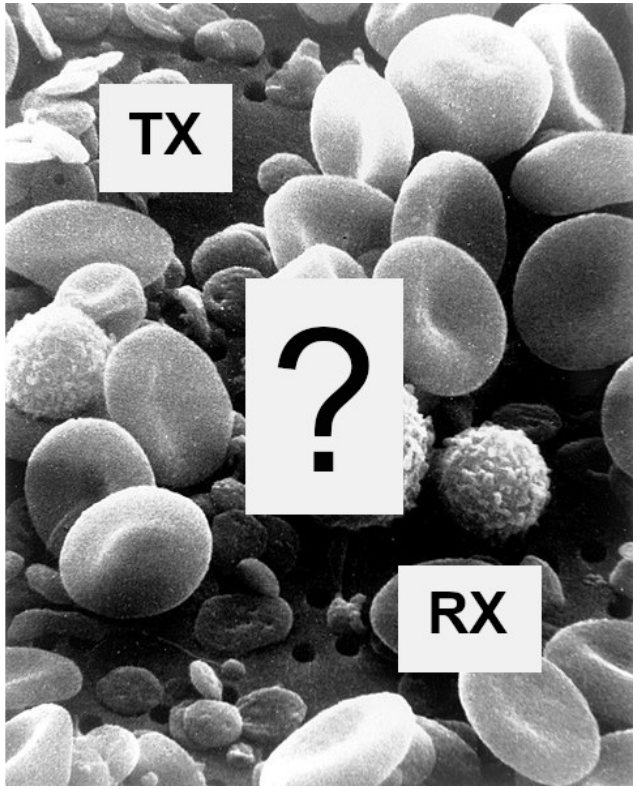


Consider cells in a living environment (e.g., bloodflow)

- What communication should we be interested in?
- Where are our TXs and RXs?

Image: https://commons.wikimedia.org/wiki/File:SEM_blood_cells.jpg (Bruce Wetzel and Harry Schaefer)

Biological Communication Networks



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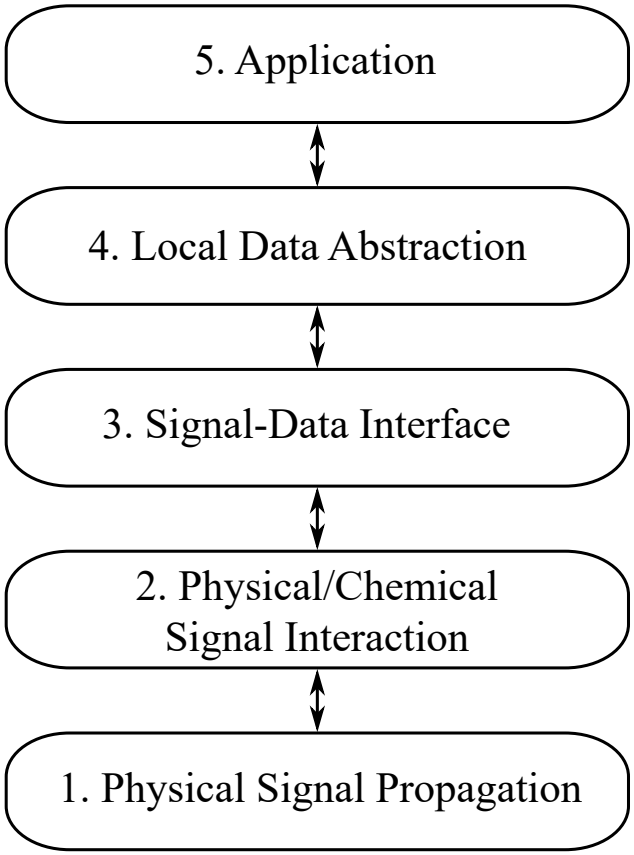
Communication Systems in Biology

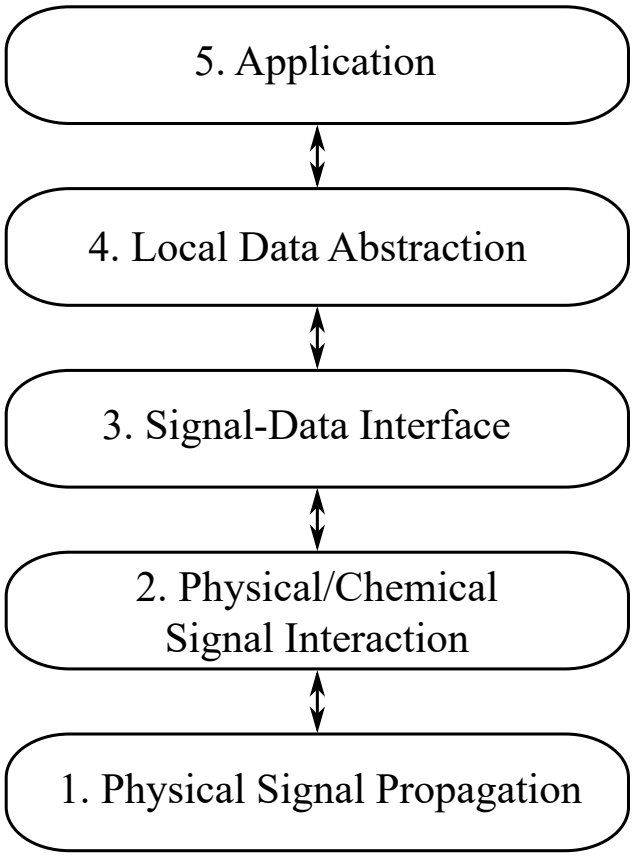
Message	TX	Environment	RX	Destination
Organelle Single Cell Tissue Organ Organism Experimenter		Cytosol Extracellular Space Circulatory System Microplate Microfluidic Channel Petri Dish Air		Organelle Single Cell Tissue Organ Organism Experimenter

Hierarchy for Cell Signaling



Bi *et al.*, *IEEE Commun. Surveys and Tutorials*, Third Quarter 2021

Hierarchy for Cell Signaling



→ The aggregate behaviour informed by signaling

→ Local significance of data

→ Conversion between signal and data

→ Signal transmission/reception processes

→ Molecule transport

- We can define the levels as appropriate for our application

Bi *et al.*, *IEEE Commun. Surveys and Tutorials*, Third Quarter 2021

Organ-on-a-Chip (OoaC)

Dr Hamidreza Arjmandi

Mitra Rezaei

AstraZeneca

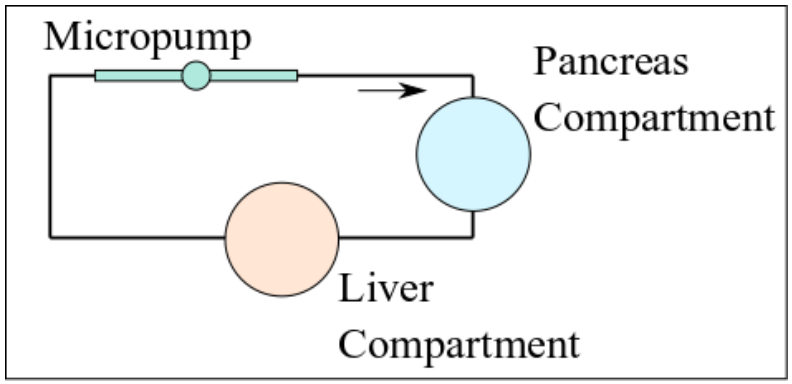
Figure: Organ-on-a-Chip platform

ex vivo microphysiological models

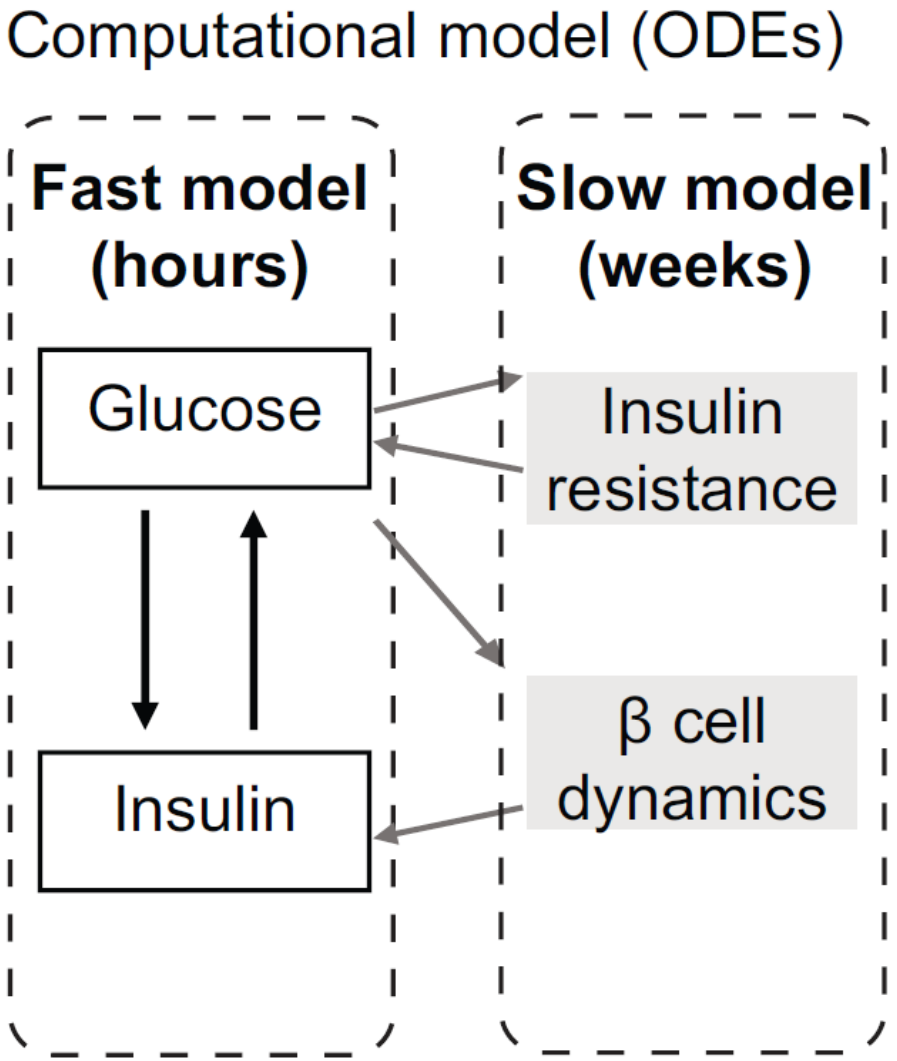
- Replicate diseased states and progression in microfluidics
- Aim to replace drug experimentation in animals
- Need to translate results to *in vivo* (in-body)

Image: Bauer *et al.*, Scientific Reports, vol. 7, 2017, https://doi.org/10.1038/s41598-017-14815-w

AZ Interest in Glucose Regulation



- Measure metabolic processes
- Experimental and mathematical models
- Being expanded to 3-organ and 4-organ models



Casas *et al.*, *bioRxiv*, August 2021, https://doi.org/10.1101/2021.08.18.456693

OoaC Problem – Spheroid Behavior

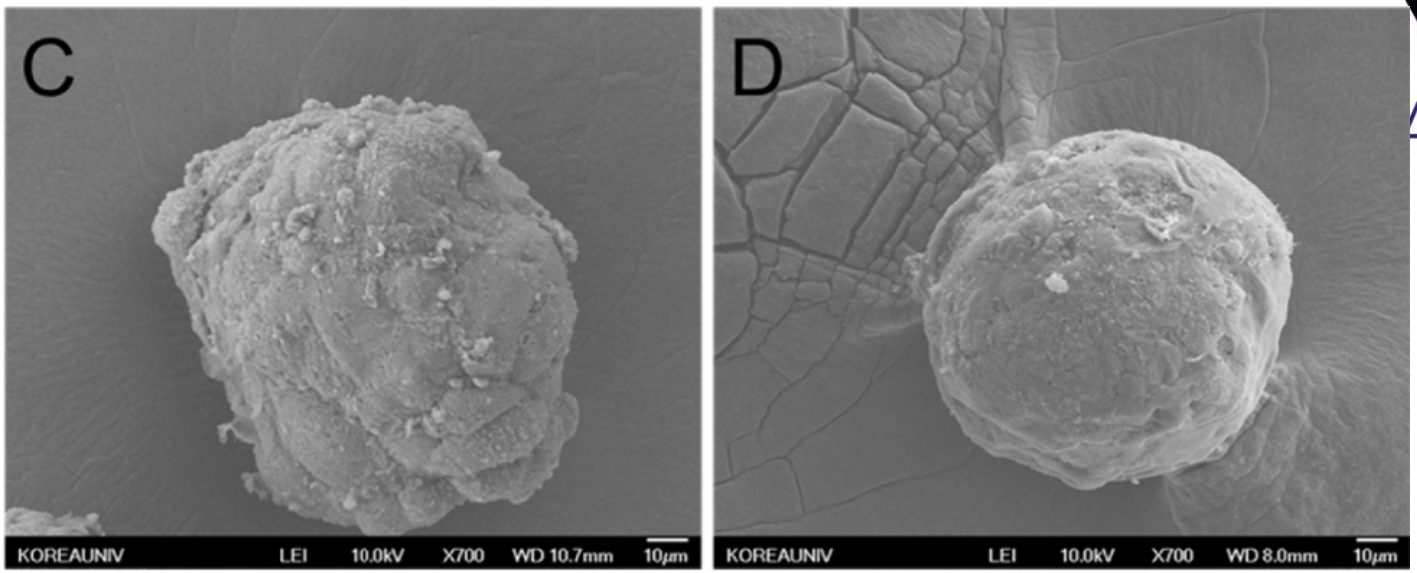


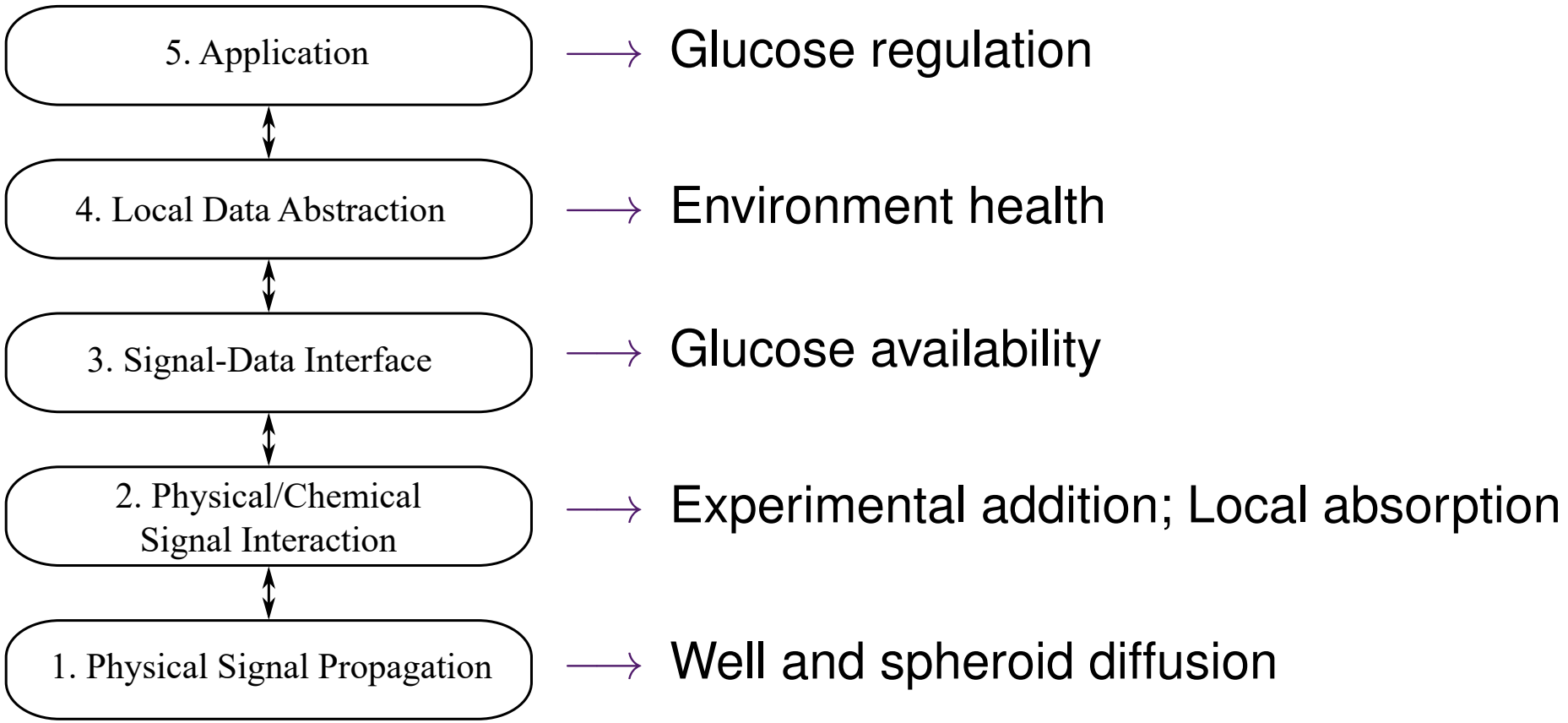
Figure: Hepatocyte (liver) spheroid after (left) 3 days; (right) 9 days

"Organs" in OooC are organoids:

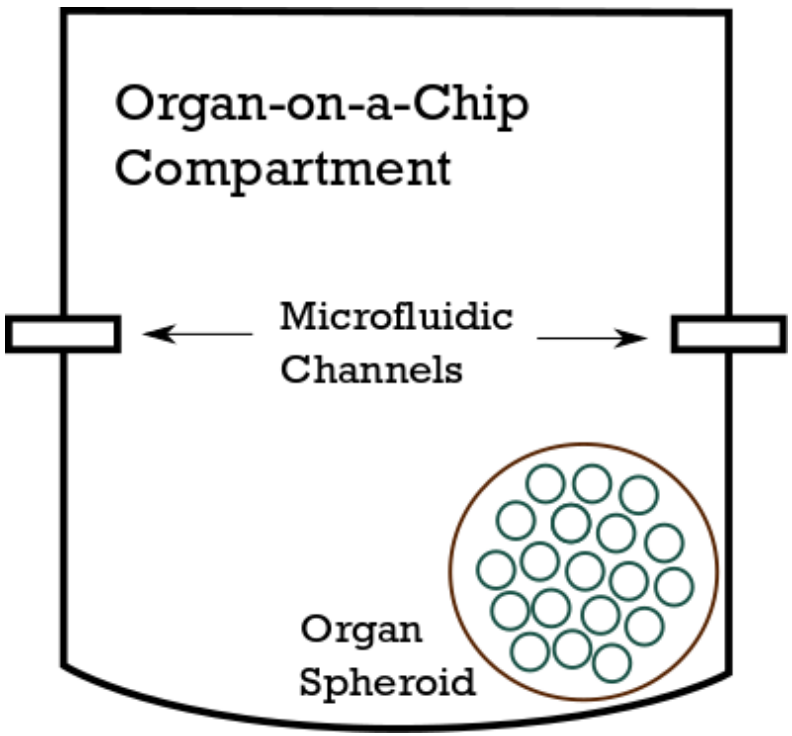
- Cells grow in dense clumps, often as **spheroids**
- Tens of thousands of **heterogeneous** cells
- Spheroids are manually handled by experimentalists
- Sensitive to surrounding fluid environment

Image: No *et al.*, *PLoS ONE*, 2012, https://doi.org/10.1371/journal.pone.0050723

Map OoaC Problem to Hierarchy



OoaC/Spheroid Questions

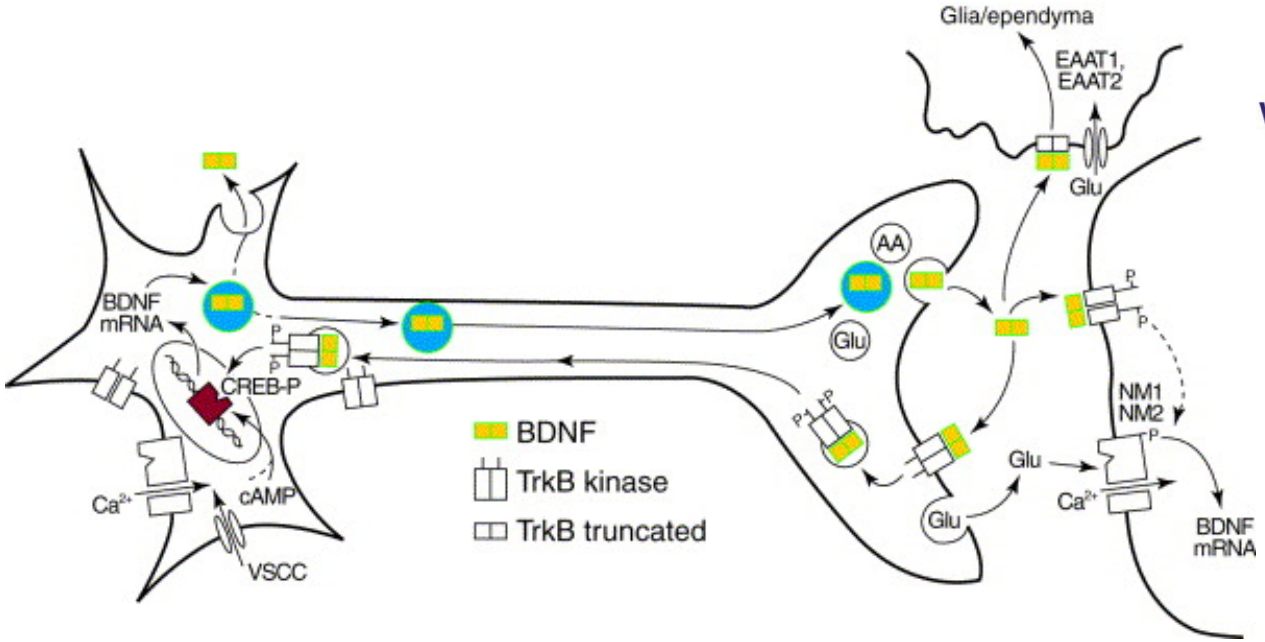


Questions we're interested in:

1. Can we model a spheroid as a TX or RX*?
2. How to describe channel impulse response?
3. Impact of concentration distribution within spheroid?
   - Potential for **necrotic core**
4. Impact of cell heterogeneity?

* Initial results to be presented in Arjmandi *et al.*, *IEEE ICC 2023*

Neuron Transport of BDNF

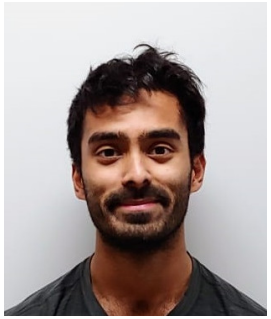


There's more than action potentials happening in neurons (!)

- *Brain derived neurotrophic factors* (**BDNFs**) support:
  - Anti-apoptosis
  - Neuron growth
  - Strengthens synapses by increasing neurotransmitter receptors
- BDNF is produced, transported, and released

Image: Altar and DiStefano, *Trends in Neurosciences*, 1998, https://doi.org/10.1016/S0166-2236(98)01273-9

Neuron Transport Problem



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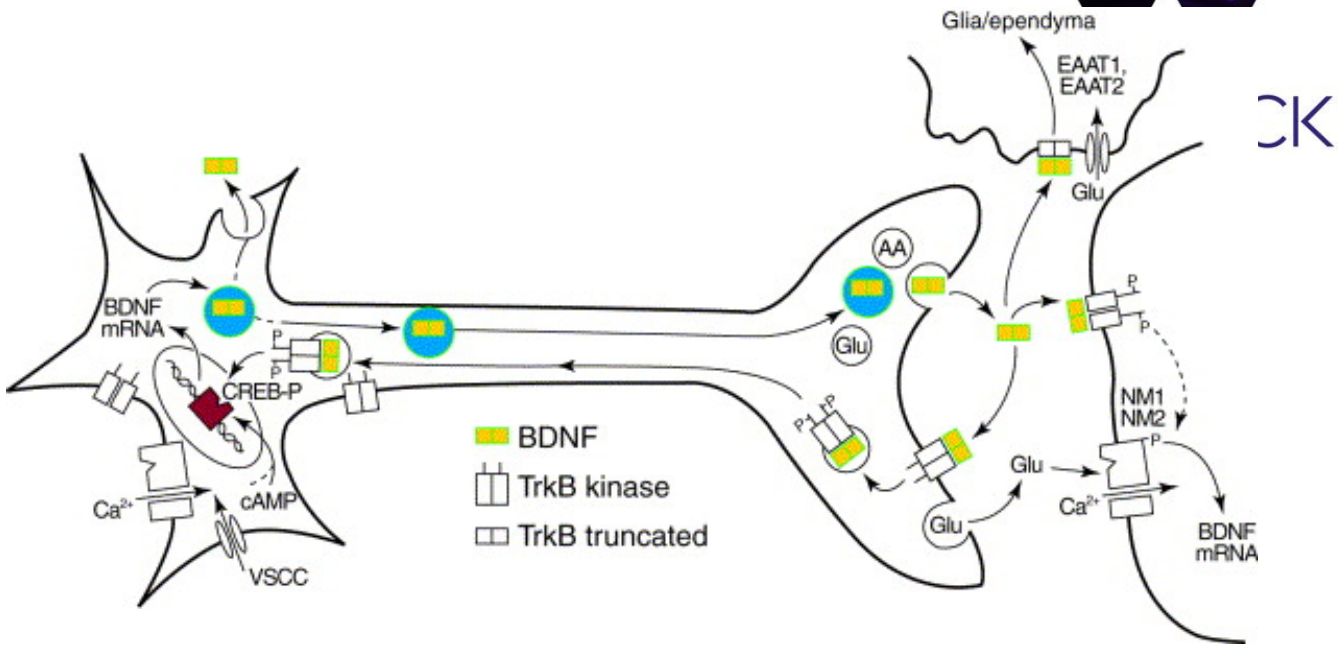
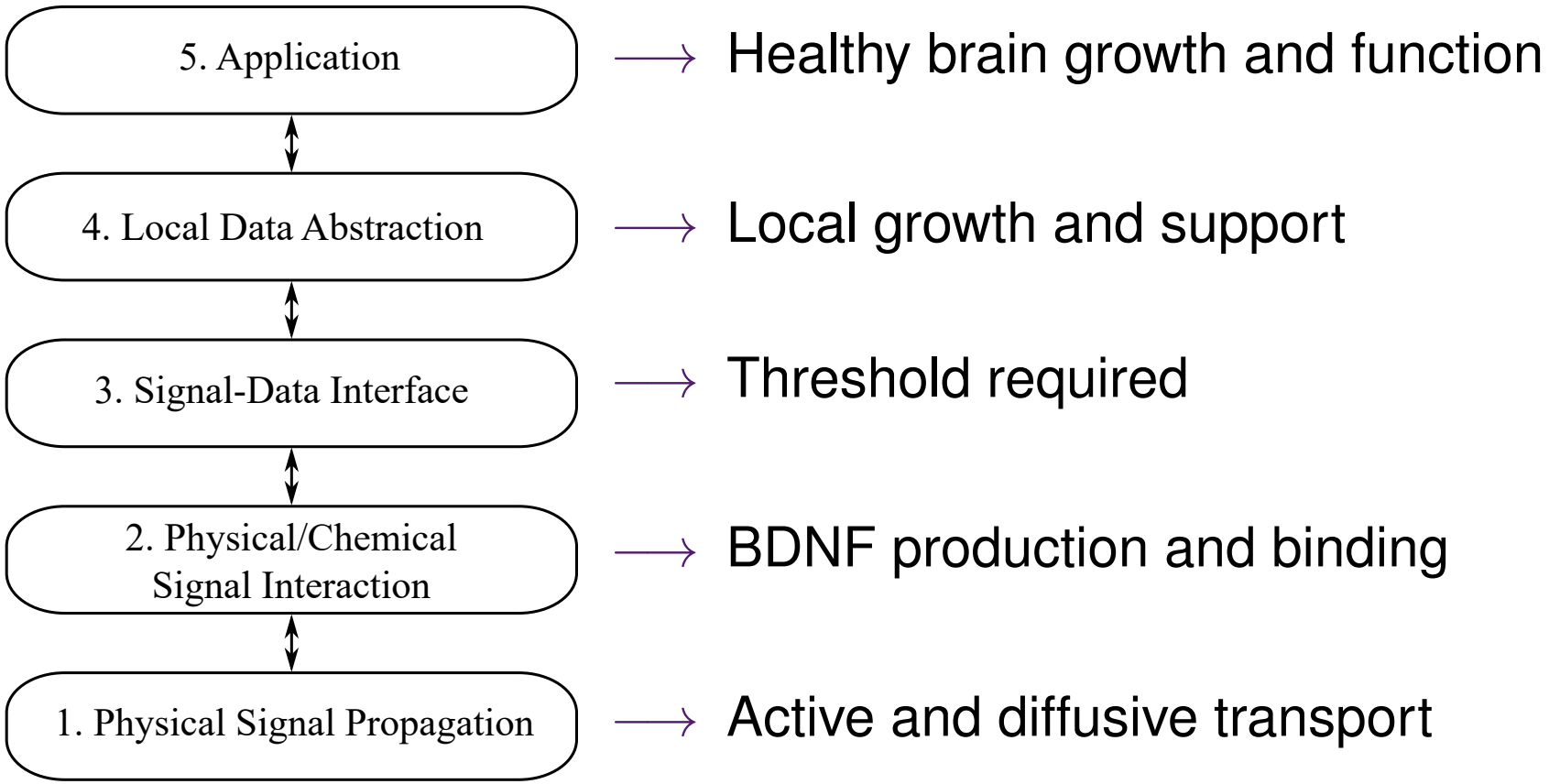


Neurodegenerative diseases are associated with BDNF degradation

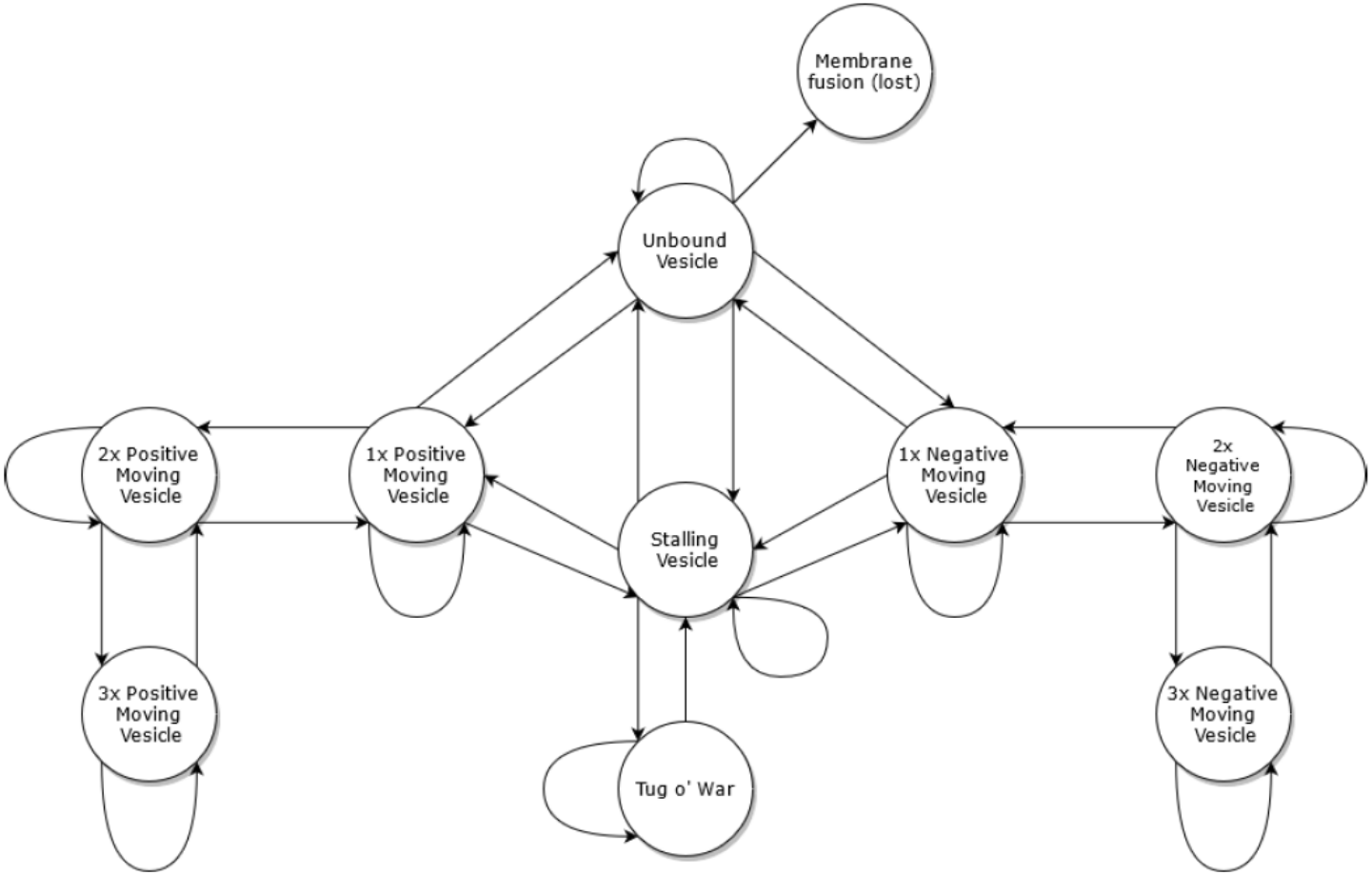
- Under Alzheimer's, BDNF transport is impeded
- Modeling BDNF as an information packet
- Can we predict neuron health and connectivity via BDNF transport?
- Combination of dry and wet-lab experimentation to track BDNF

Image: Altar and DiStefano, *Trends in Neurosciences*, 1998, https://doi.org/10.1016/S0166-2236(98)01273-9

Map BDNF Problem to Hierarchy



BDNF Modeling



We modeled BDNF transport along axon as Markov chain

- Model generates trajectories consistent with experiments
- Transition probabilities predicted by fitting experimental data to Viterbi algorithm

Bacteria Colonies

Dr Hamidreza Arjmandi

Dr Ibrahim Isik

Yanahan Paramalingam

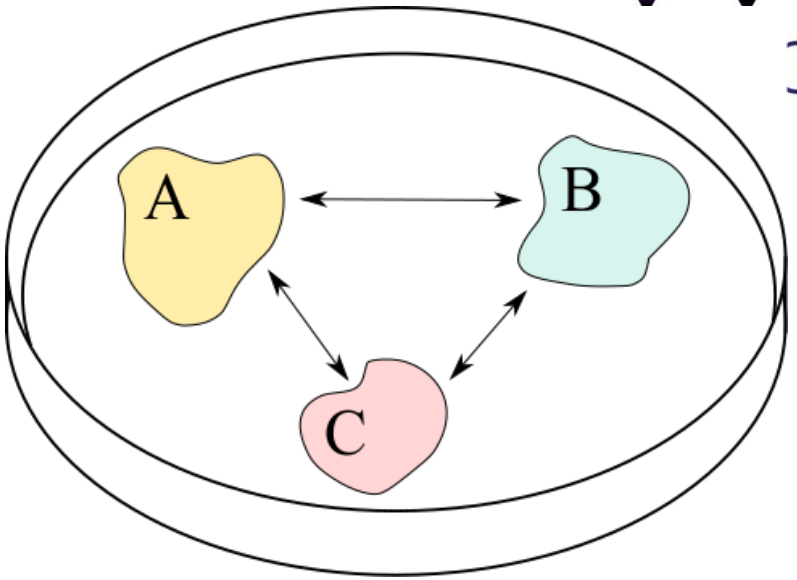


Figure: Bacteria on a plate

We can grow diverse bacteria colonies over agar in plates

- Variants with different antibiotic production and responses
- Colonies can respond to stimulating molecules and to each other
  - We ask: How do these molecules propagate?
- Big question: how to instigate production of new antibiotics?

Biofilms

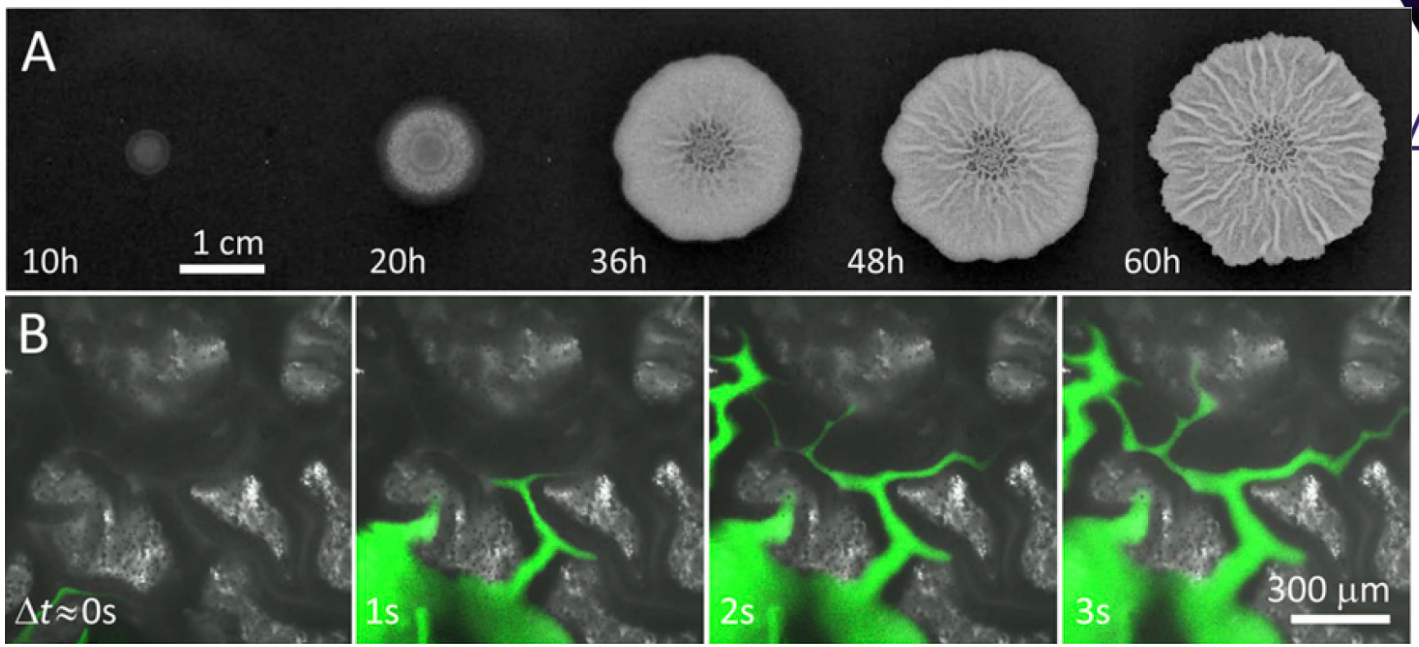


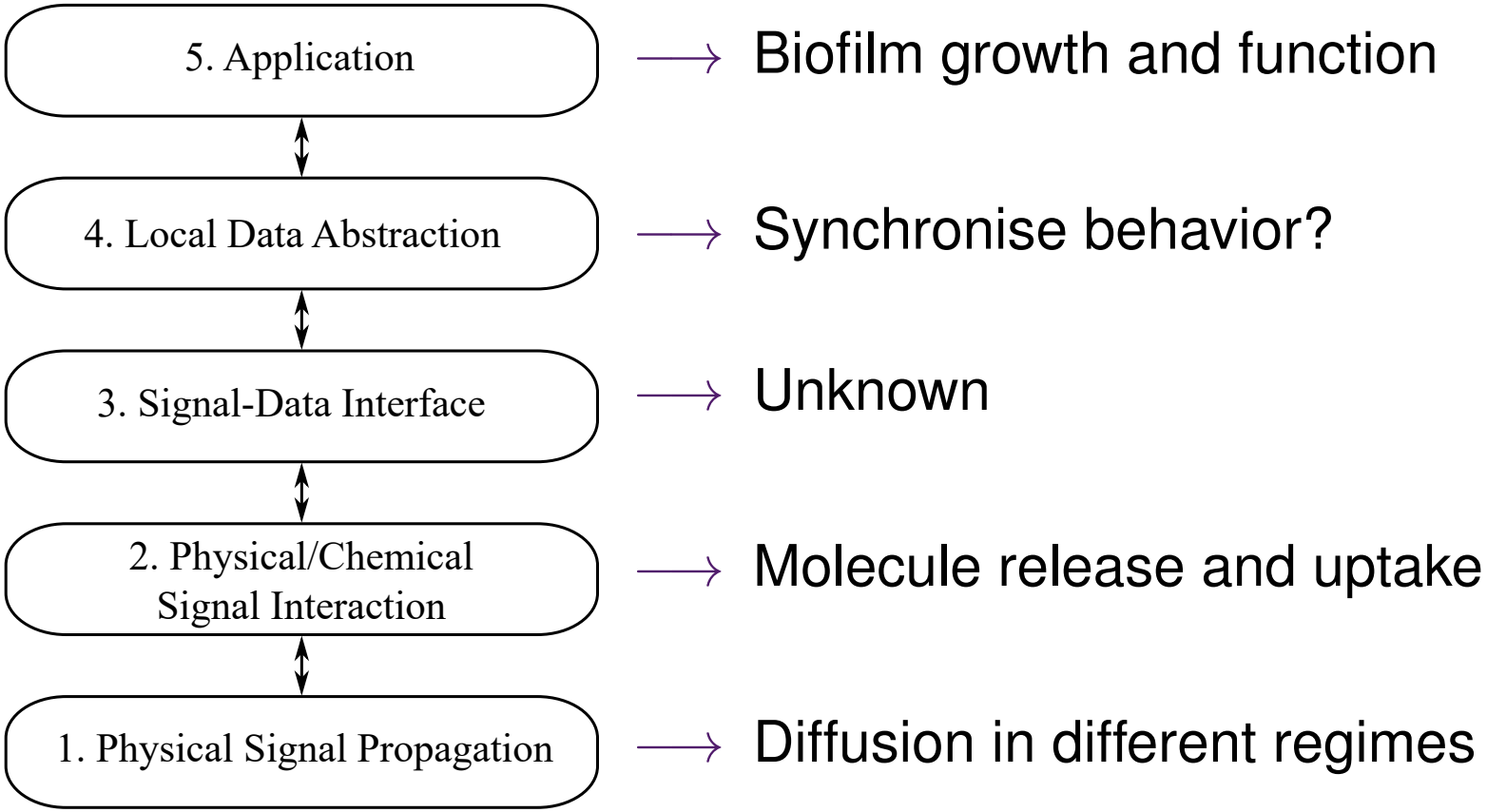
Figure: Biofilm of *Bacillus subtilis*

Consider behavior within single colony (**biofilm**)

- Some species have sophisticated internal geometry
- Water channels enable molecule transport and some mobility
- Heterogeneous signal propagation (inside/outside channels)

Image: Wilking *et al.*, *PNAS*, Jan. 2013, https://doi.org/10.1073/pnas.1216376110

Map Biofilm Transport to Hierarchy



Biofilm Questions

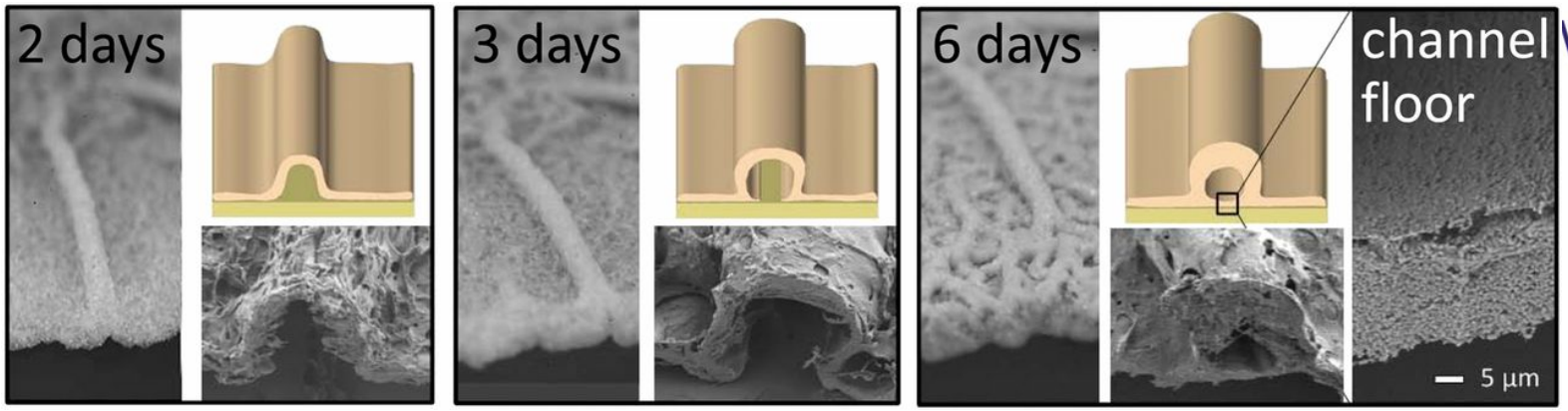


Figure: Water channel formation of *Bacillus subtilis*

We have questions about the role of water channels:

- What are the communications benefits of water channels?
- Is water channel placement solving an optimization problem?
- Can changes in geometry be justified by changing priorities?

Image: Wilking *et al.*, *PNAS*, Jan. 2013, https://doi.org/10.1073/pnas.1216376110

Conclusions

WARWICK

Communication methods can be adapted to model cell biology

- Many practical applications rely on molecular communication

Hierarchy gives us language for describing biological communication

- Layering approach can be used at different scales

Case studies demonstrate open problems and interdisciplinarity

- Overall theme: **New channels to model**
- Applying over scales *much larger* than prevalent MC literature

The End

www.warwick.ac.uk/adamnoel

Research support: