# Developing Modern Mathematical Theories and Computational Tools for Complex Biological Systems

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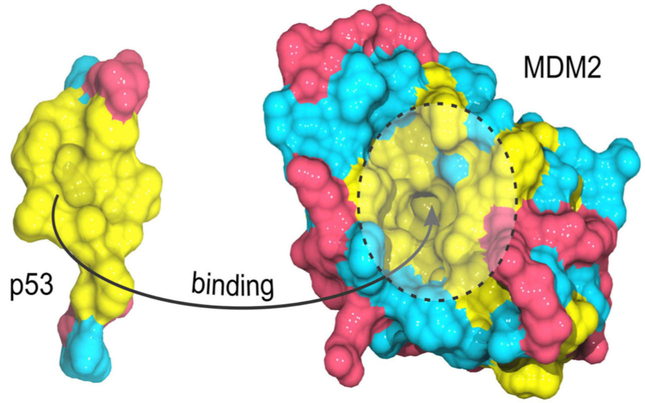
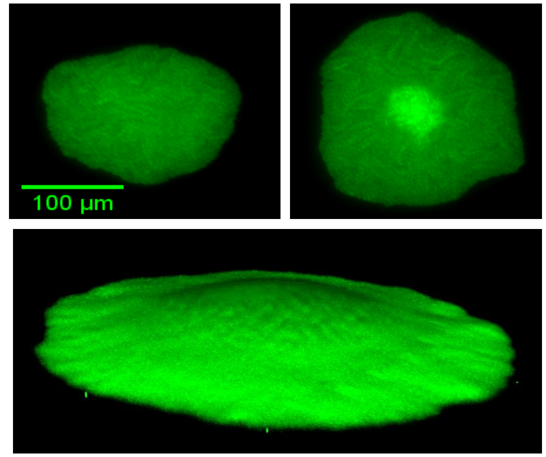
**Math, UCSD**

**The Lattimers Fellowship Lecture**
**Division of Physical Sciences, UCSD**
**December 16, 2020**

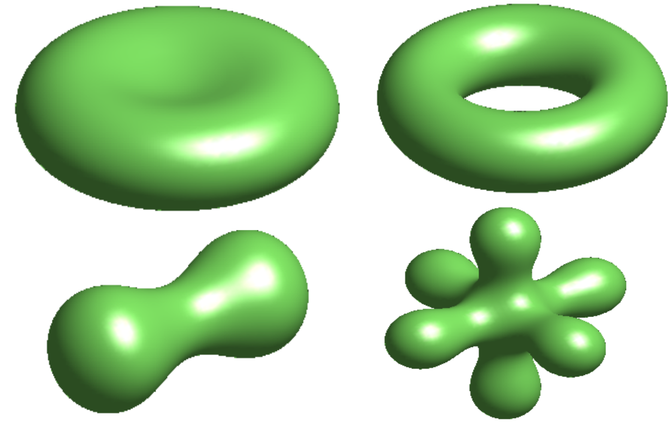
**Thank You, George and Carol!**

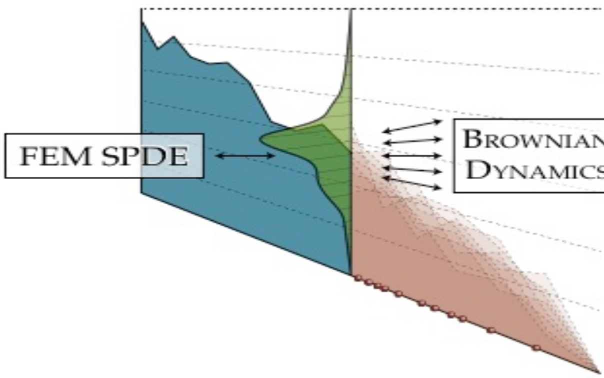


molecular recognition

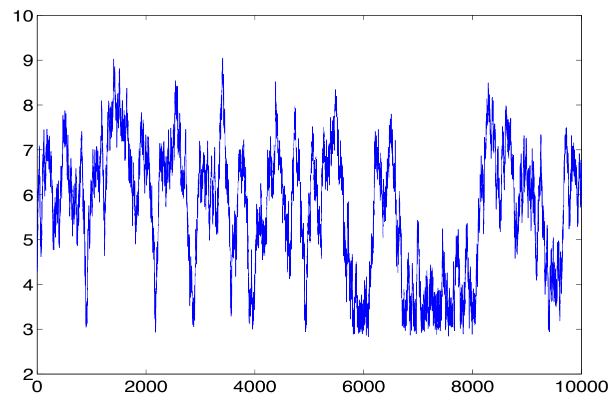


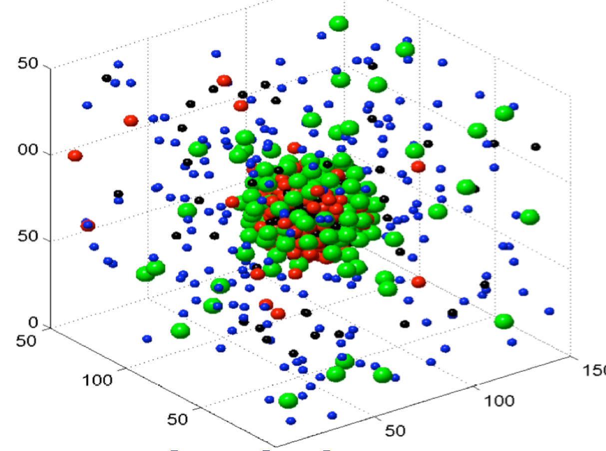
bacterial colony

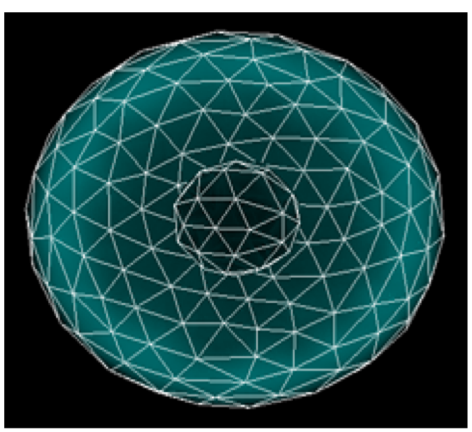

membranes/vesicles

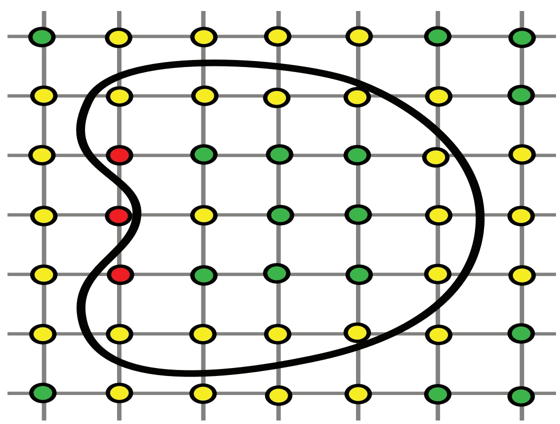


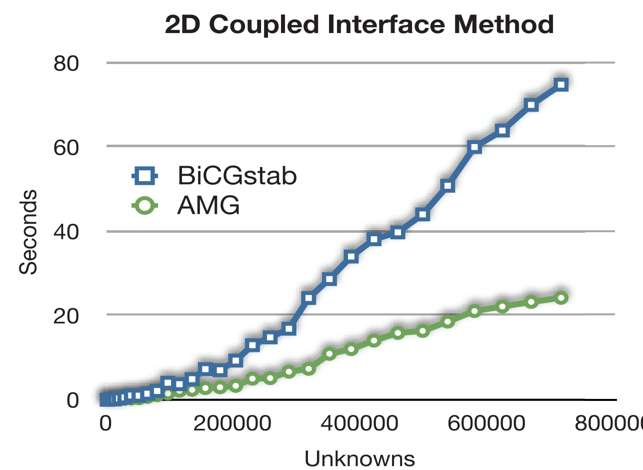
multiscale models


stochastic models


simulations


surfaces/interfaces


soln's of diff. eqns



fast algorithms

# Spatiotemporal Dynamics of Bacterial Colony Growth with Cell-Cell Mechanical Interactions

- Explain experimental findings.
- Identify key parameters.
- Understand the genetic origins.

**Collaboration with Hwa's group at UCSD and Sun's group at Cal State U - Long Beach. New NSF grant.**

**Linear radial growth** (Pirt 1967)

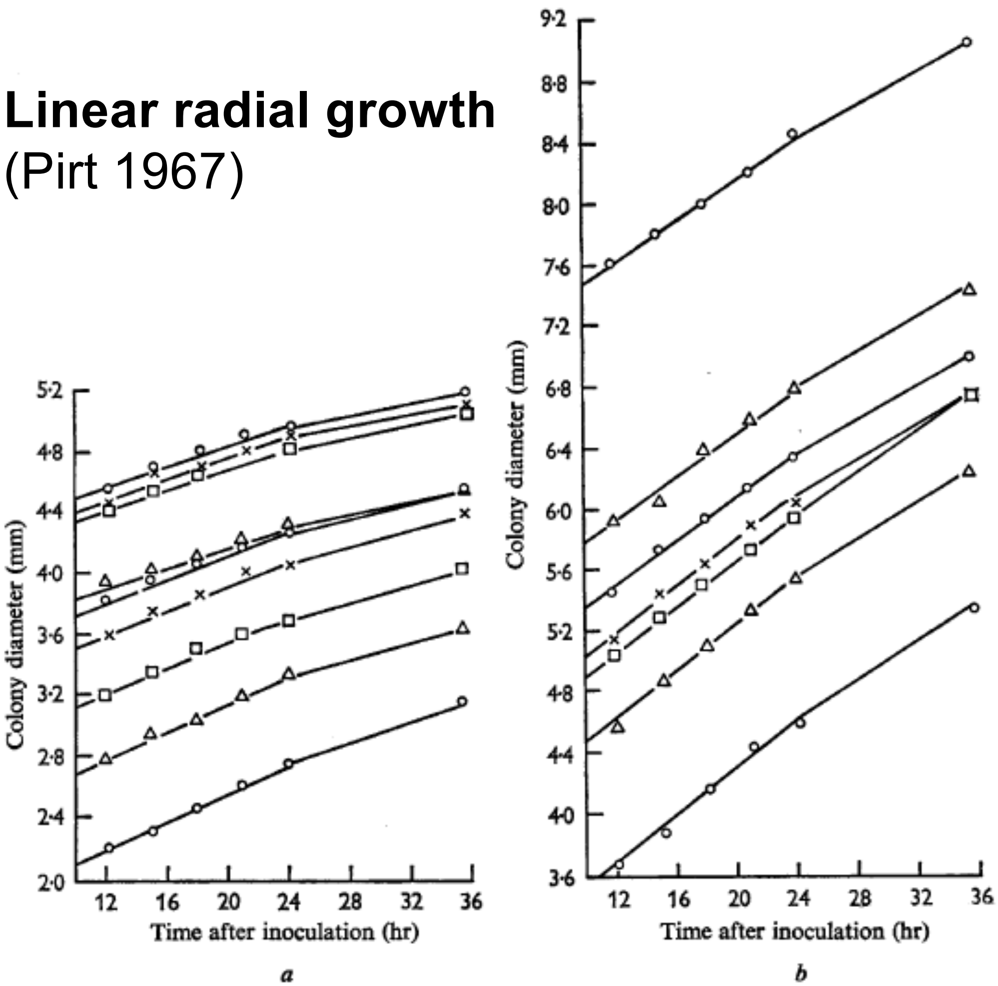
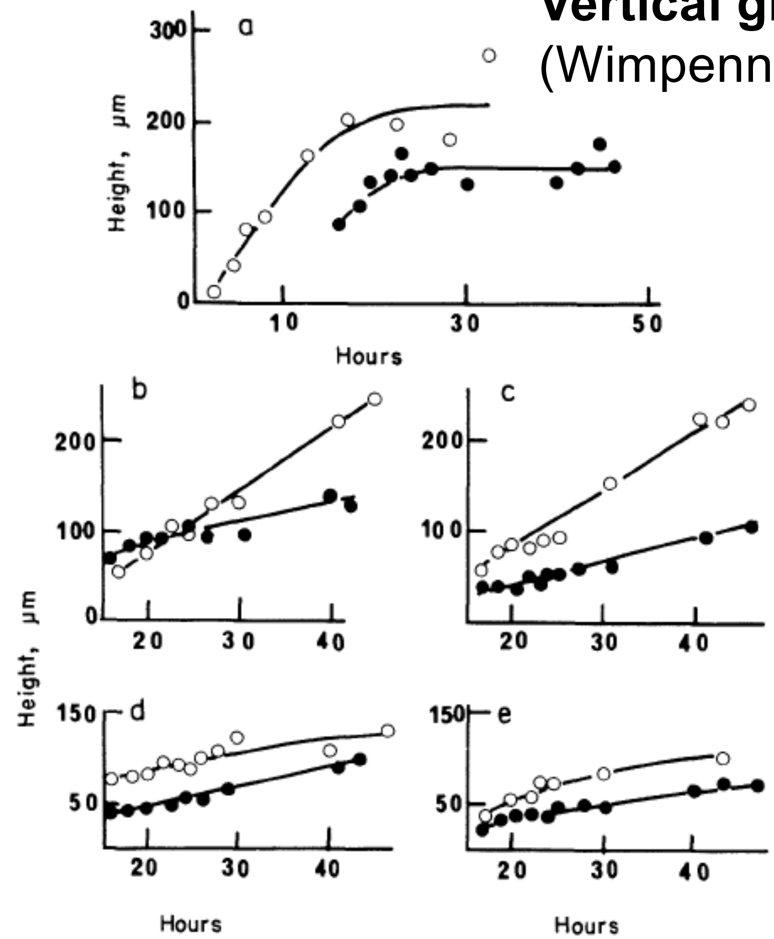


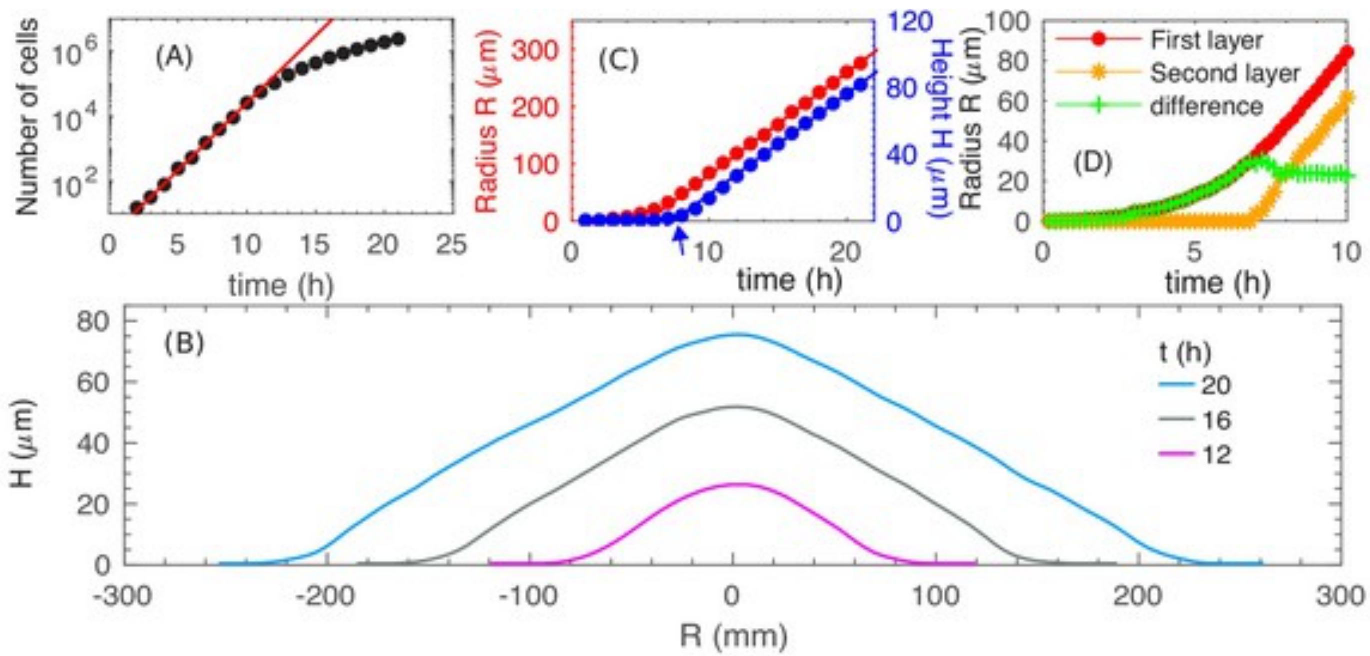

Fig. 2. Rates of increase in the diameters of *Escherichia coli* colonies on nutrient agar: (*a*) glucose, 1·28 g./l.; (*b*) glucose, 5·12 g./l. Medium DMA; temperature 37°.

**Vertical growth** (Wimpenny 1981)

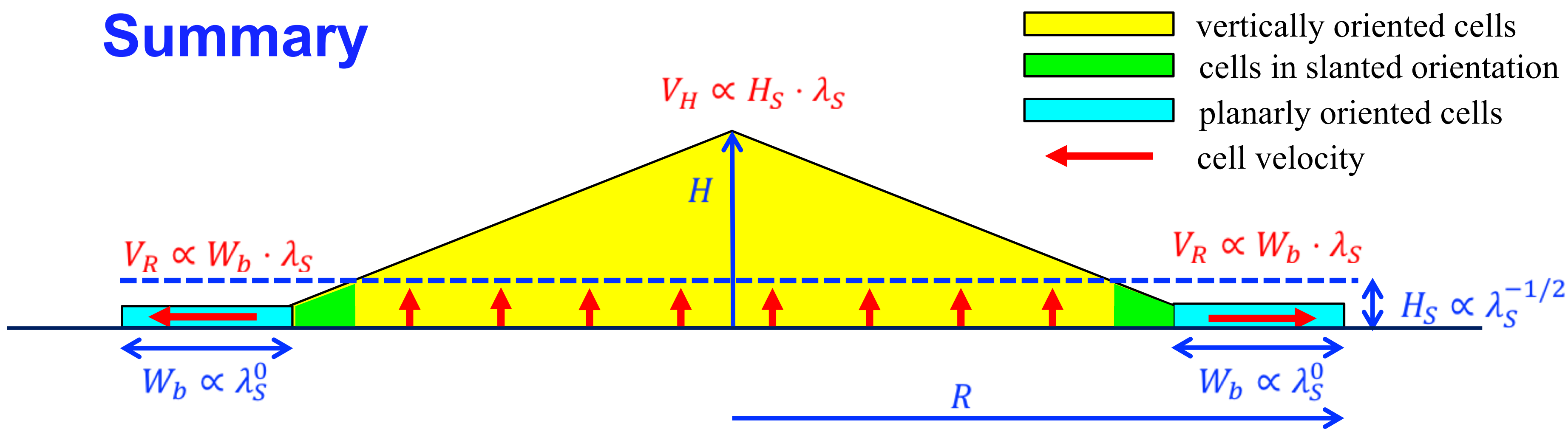



Aerobic (circle) and anaerobic (dots) growth.

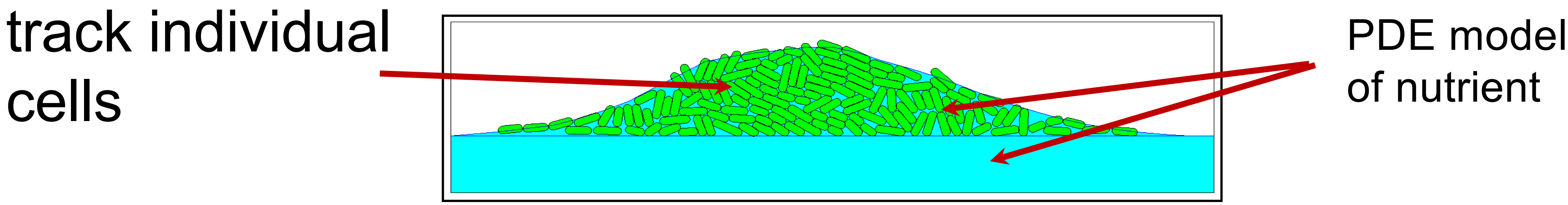
# Theory and simulations

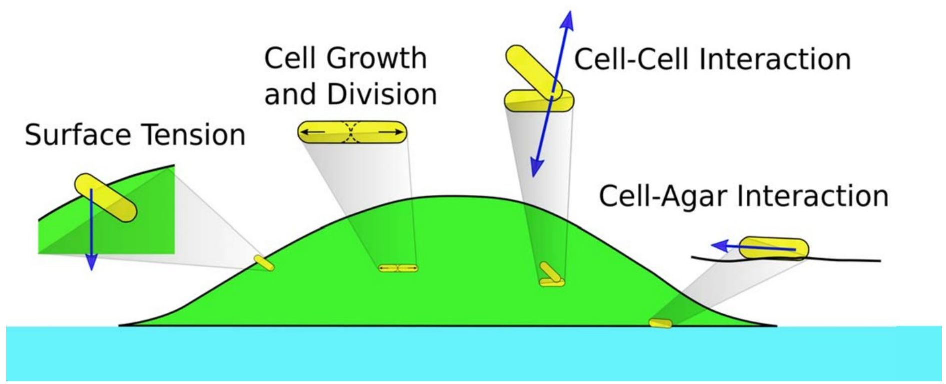


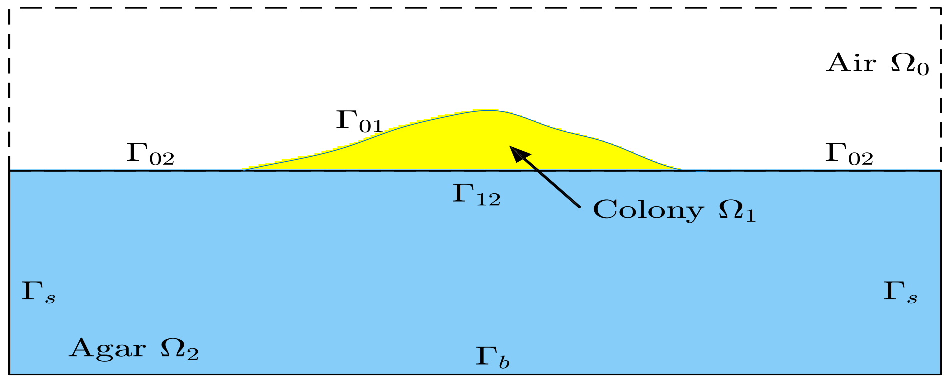

# Summary



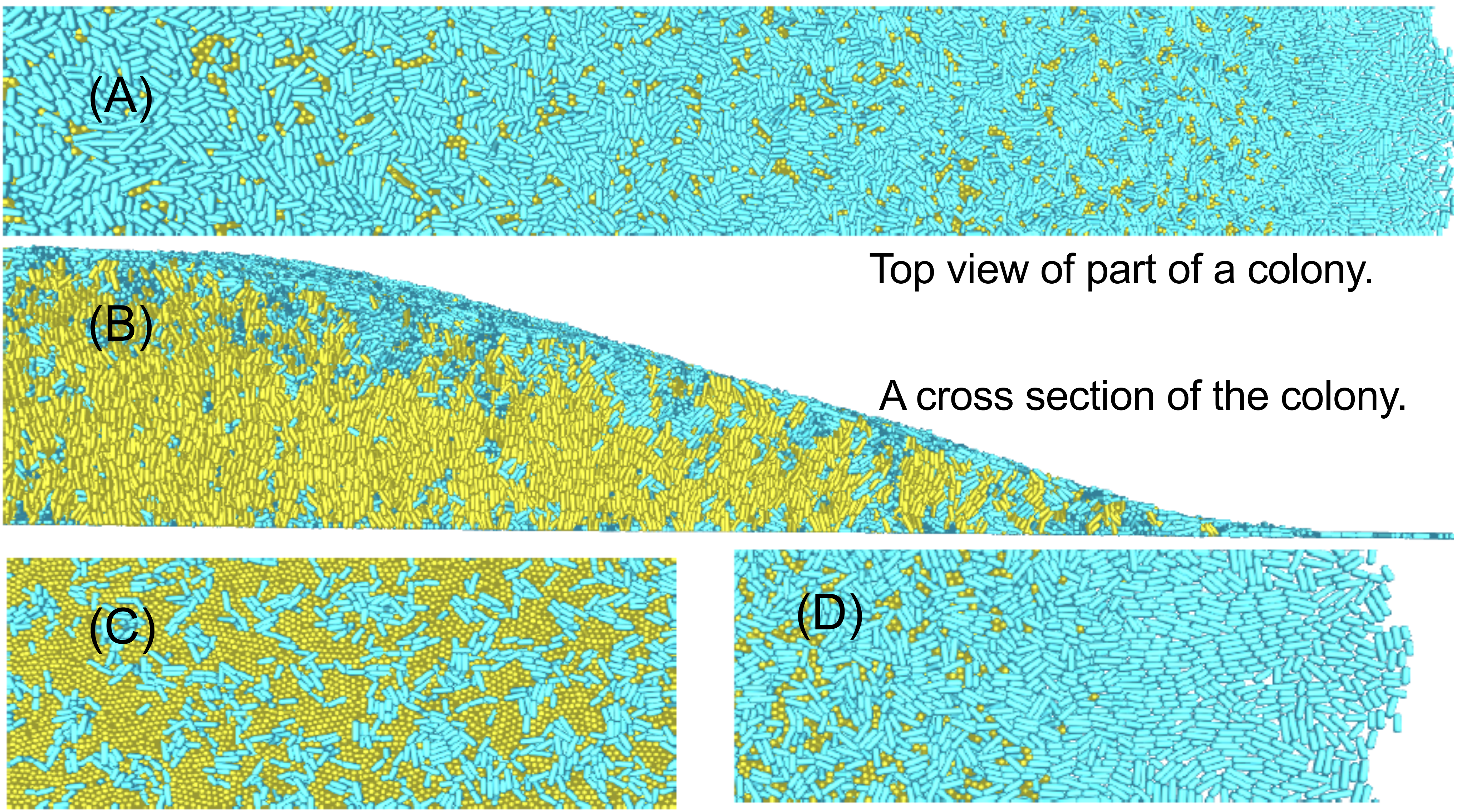
# Approach: A Two-Scale Model and Simulations



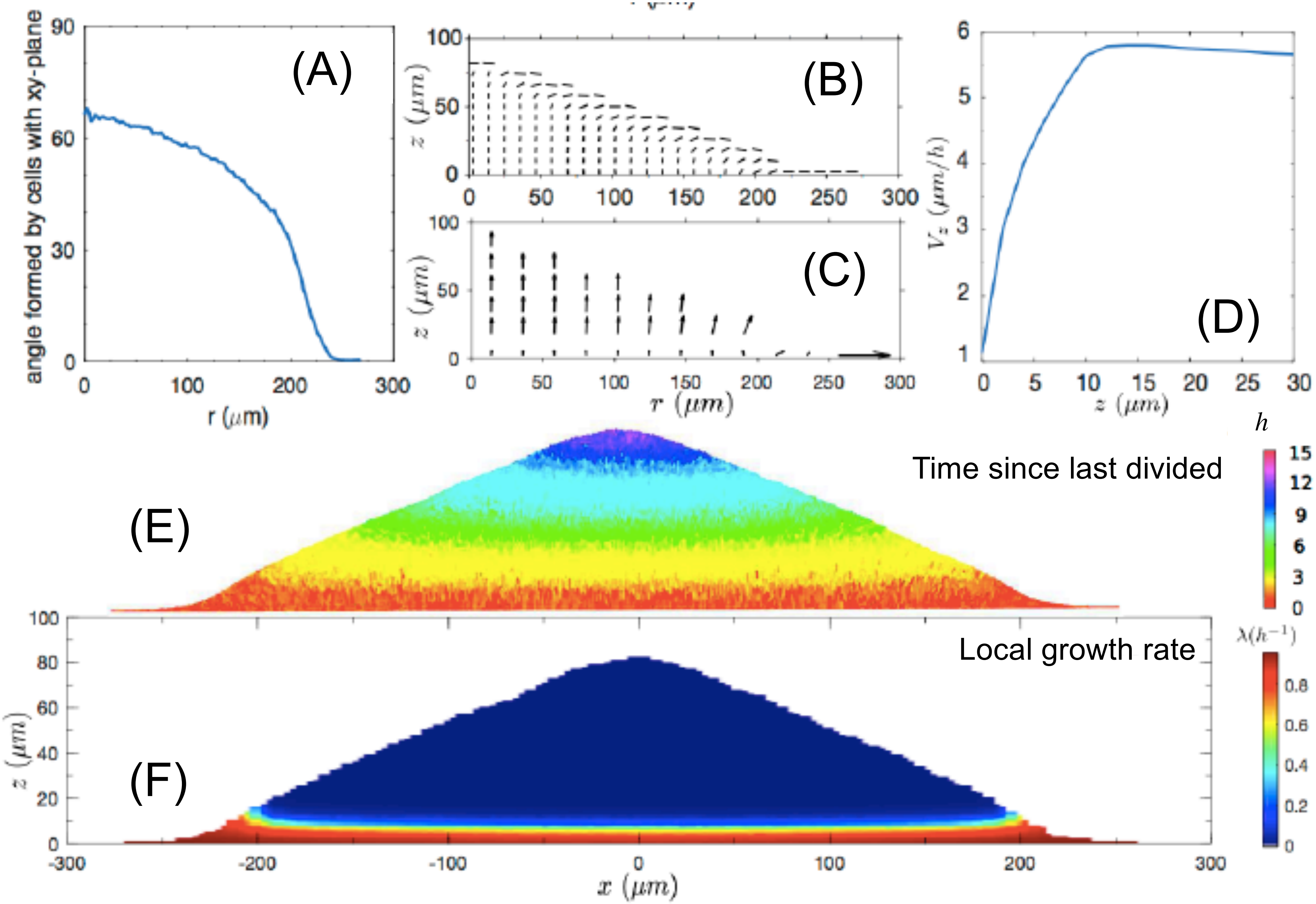
Cyan cells: large angles with the z-axis.  Golden cells: smaller angles.




Bottom view of a central part.

Bottom view of a  periphery part.

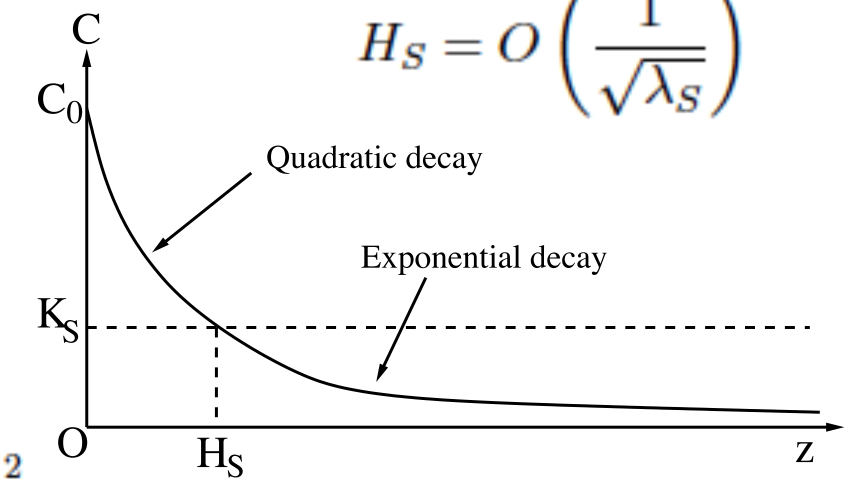
# Vertical Growth: Orientation and Growth Zone



# A 1D model for the nutrient penetration level and growth zone

$$D_+ C''(z) = \frac{\rho_0 \lambda_S}{Y} \frac{C}{C + K_S} \qquad \text{for } z > 0$$

$$C(0) = C_0 \qquad \text{and} \qquad C(\infty) = 0$$




$$H_S = O\left(\frac{1}{\sqrt{\lambda_S}}\right)$$

In a non-dimensionalized form

$$\tilde{C}(\tilde{z}) \le e^{-\sqrt{2/3}(\tilde{z} - \tilde{z}_0)} \qquad \forall \tilde{z} \ge \tilde{z}_0$$

$$\left(\sqrt{\tilde{C}_0} - \frac{1}{\sqrt{2}}\tilde{z}\right)^2 \le \tilde{C}(\tilde{z}) \le \left(\sqrt{\tilde{C}_0} - \sqrt{\frac{\ln(e/2)}{2}}\tilde{z}\right)^2 \qquad \forall \tilde{z} \in [0, \tilde{z}_0].$$

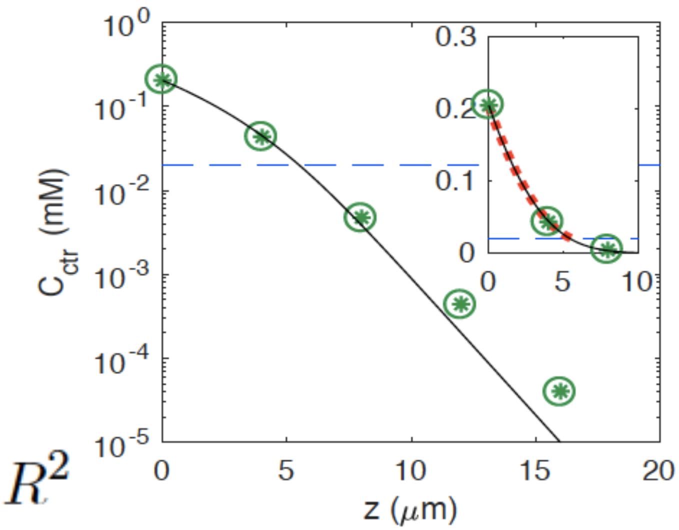



Fig. 3D simulations (green *) and 1D prediction (line or circle): semi-log plots.

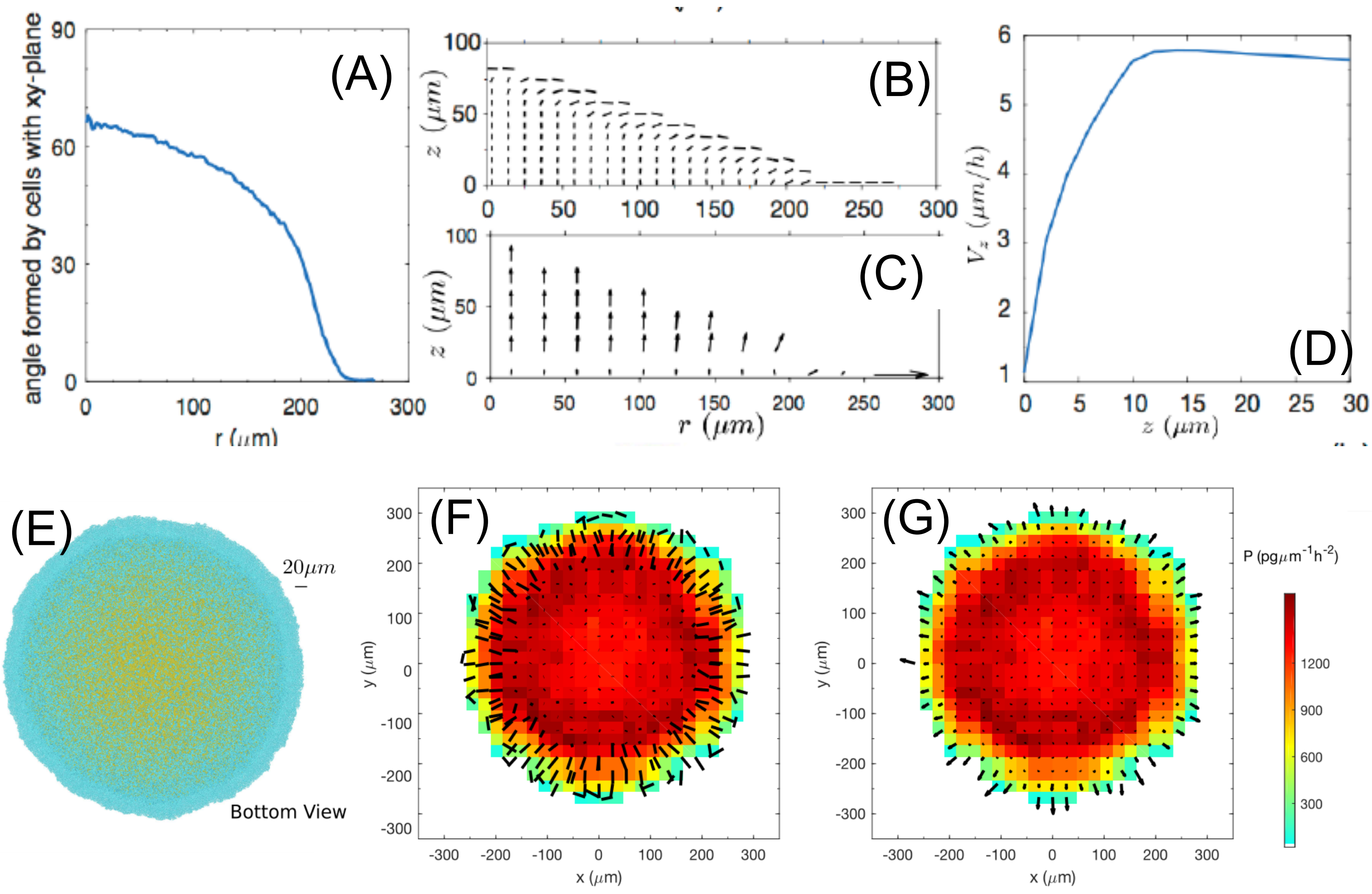
**Linear vertical growth: $V_H \propto H_S \lambda_S$.**

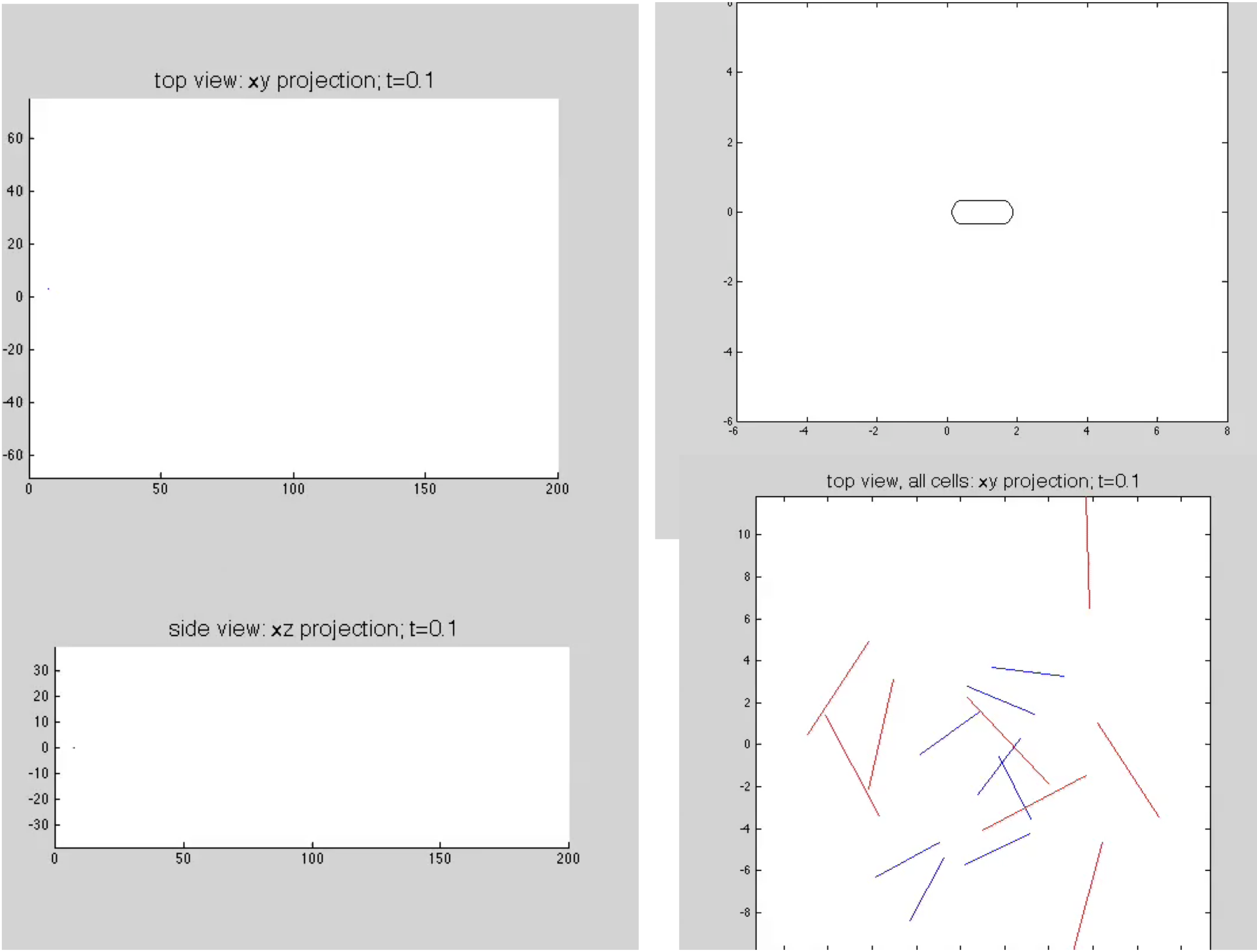
$$V_{\text{colony}} \propto R^2 H \propto R^3 \Rightarrow V_{\text{growth}} \propto \frac{d}{dt} V_{\text{colony}} \propto R^2$$

⇒ A disk of thickness $H_S$

⇒ Vertical ascending speed $V_H \propto H_S \lambda_S$

# Radial Growth: Only cells in a ring at the edge grow radially.



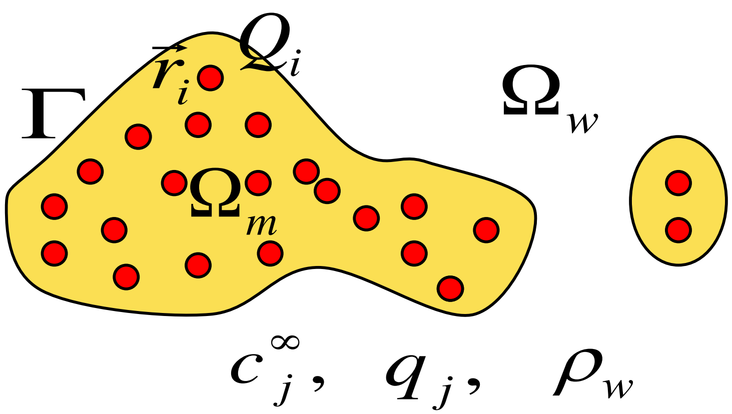

top view: xy projection; t=0.1
side view: xz projection; t=0.1
top view, all cells: xy projection; t=0.1

# Modeling and Simulations of Molecular Interactions
## (with J. A. MaCammon, L.-T. Cheng, J. Dzubiella, etc.)

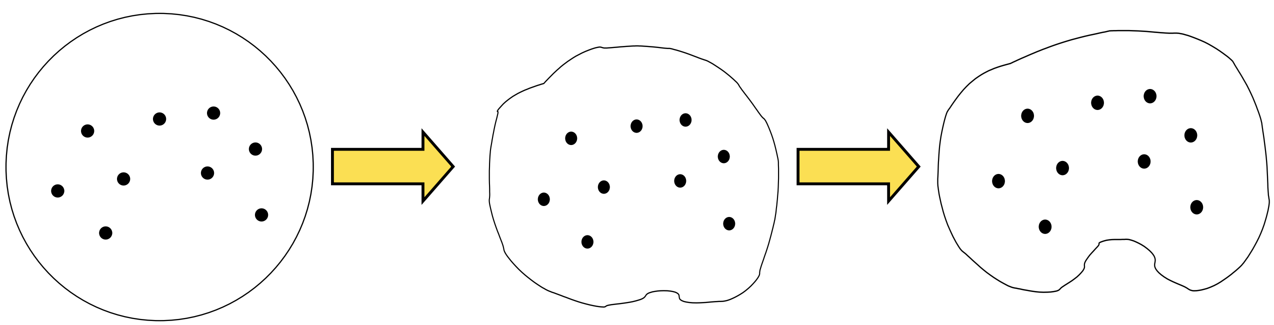
## Variational Implicit-Solvent Model (VISM)

### Free-energy functional

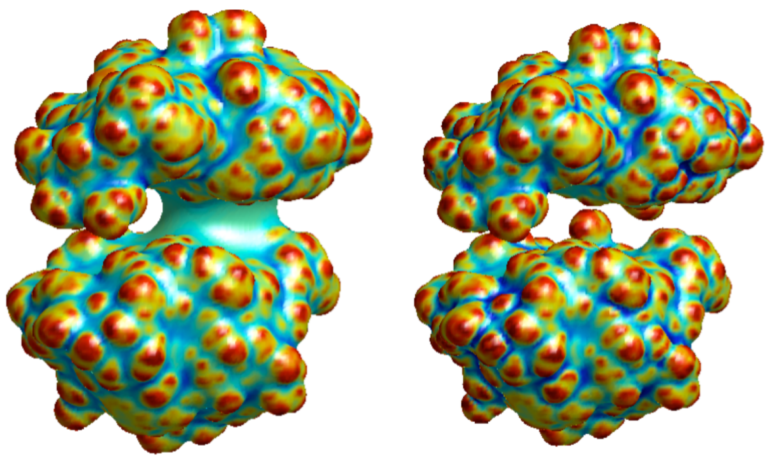
$$G[\Gamma] = P\,vol(\Omega_m) + \gamma_0 \int_{\Gamma} (1 - 2\tau H)\, dS$$
$$+ \rho_w \int_{\Omega_w} \sum_i U_{LJ,i}(|\vec{r} - \vec{r}_i|)\, dV + G_{elec}[\Gamma]$$



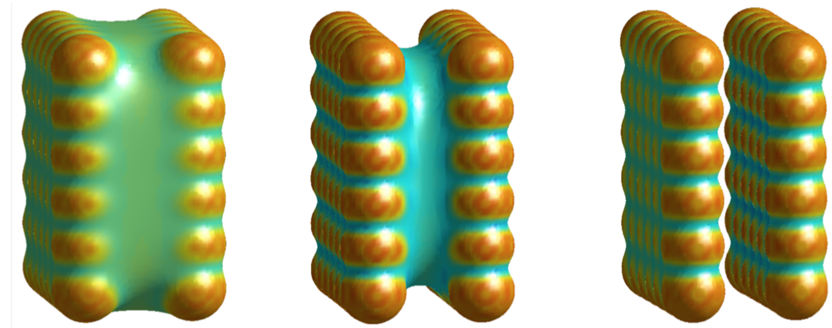

### The level-set method



## BphC

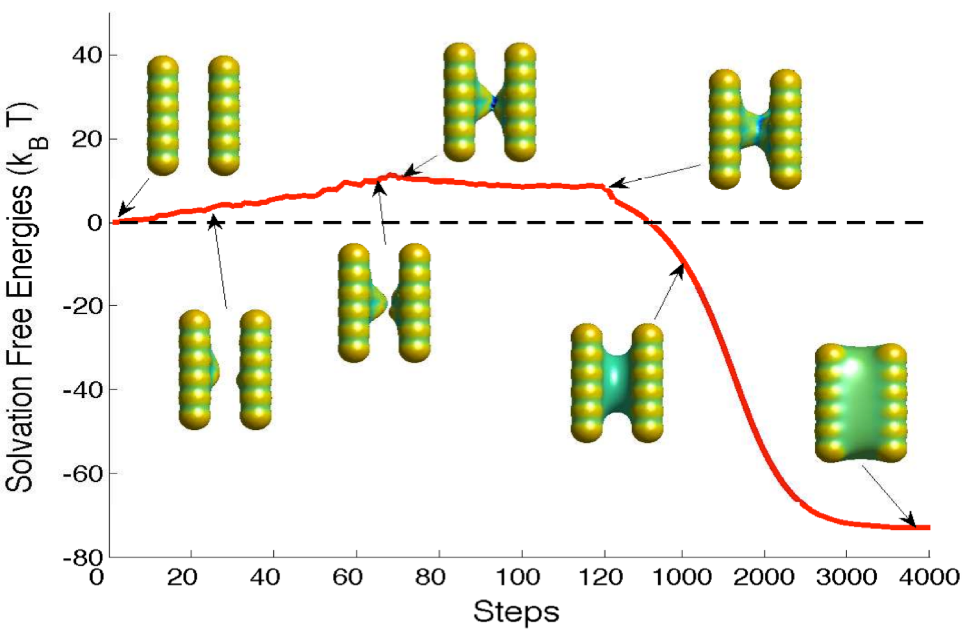


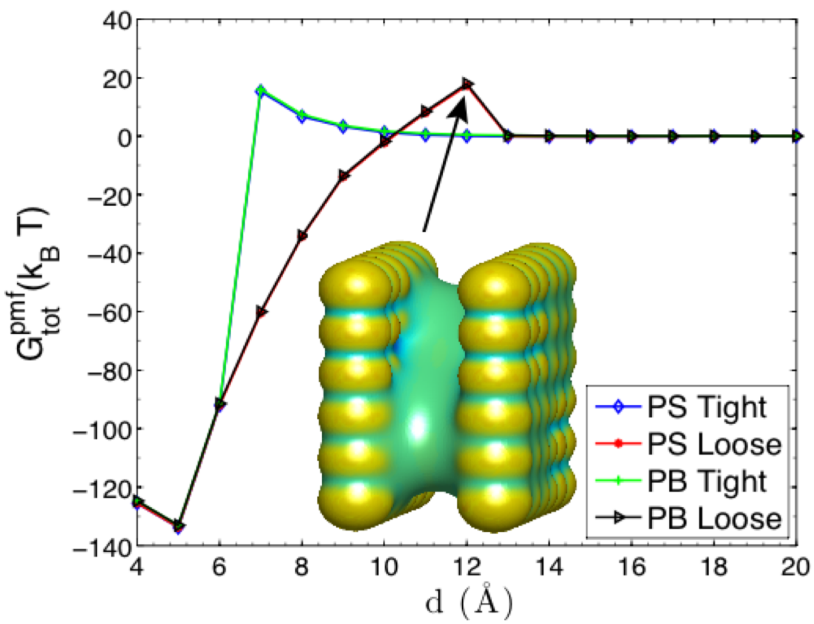
## Two charged paraffin plates



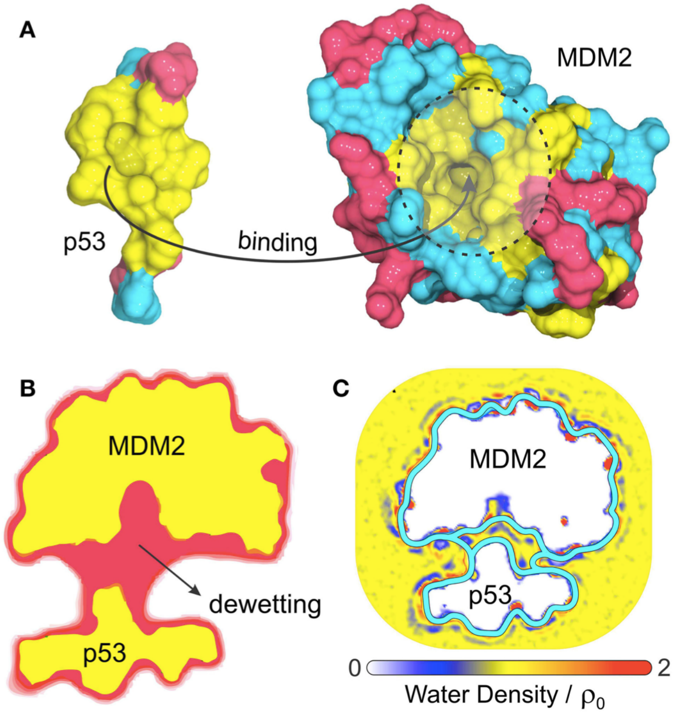
Left: no charges.
Middle: partial charges (0.2 e, 0.2 e).
Right: partial charges (0.2 e, -0.2 e).
Color represents mean curvature.

## Stochastic level-set VISM for dewetting transition

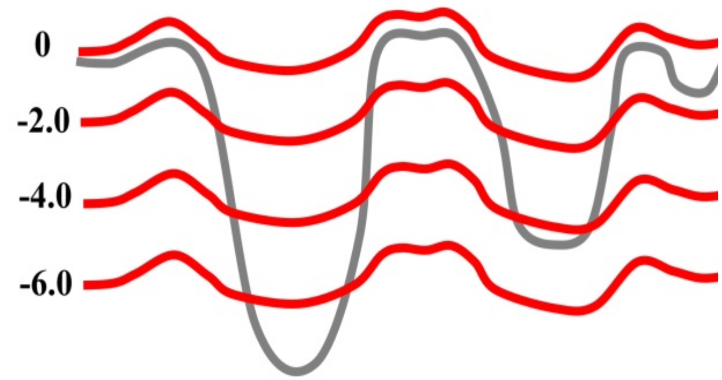


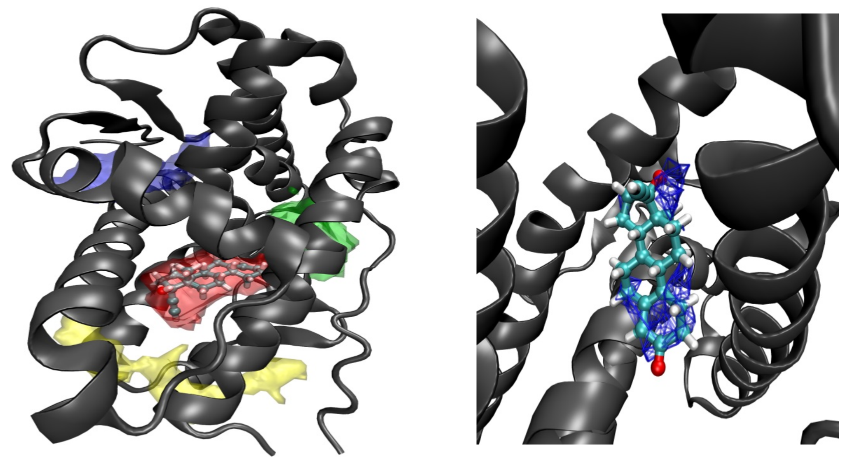



# p53/MDM2



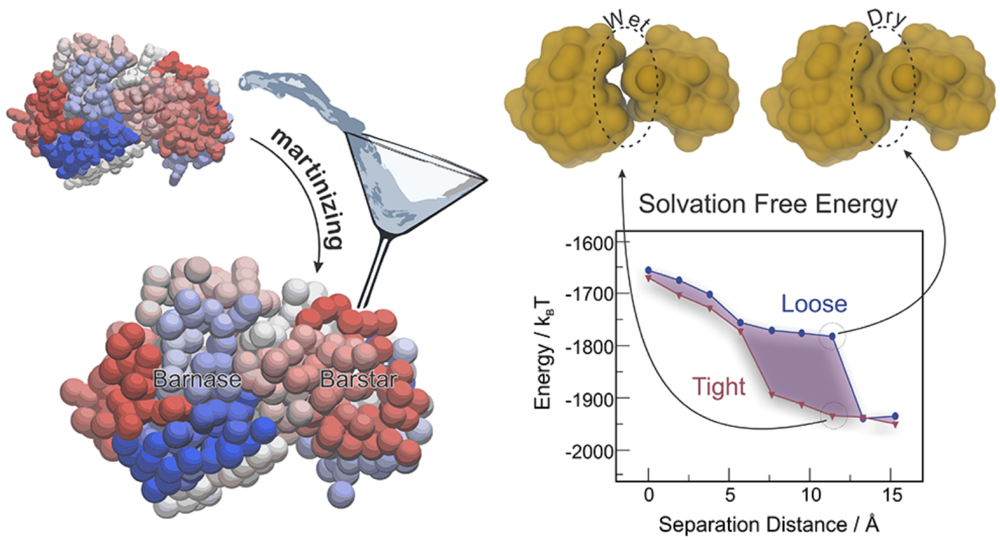

# Identifying binding sites



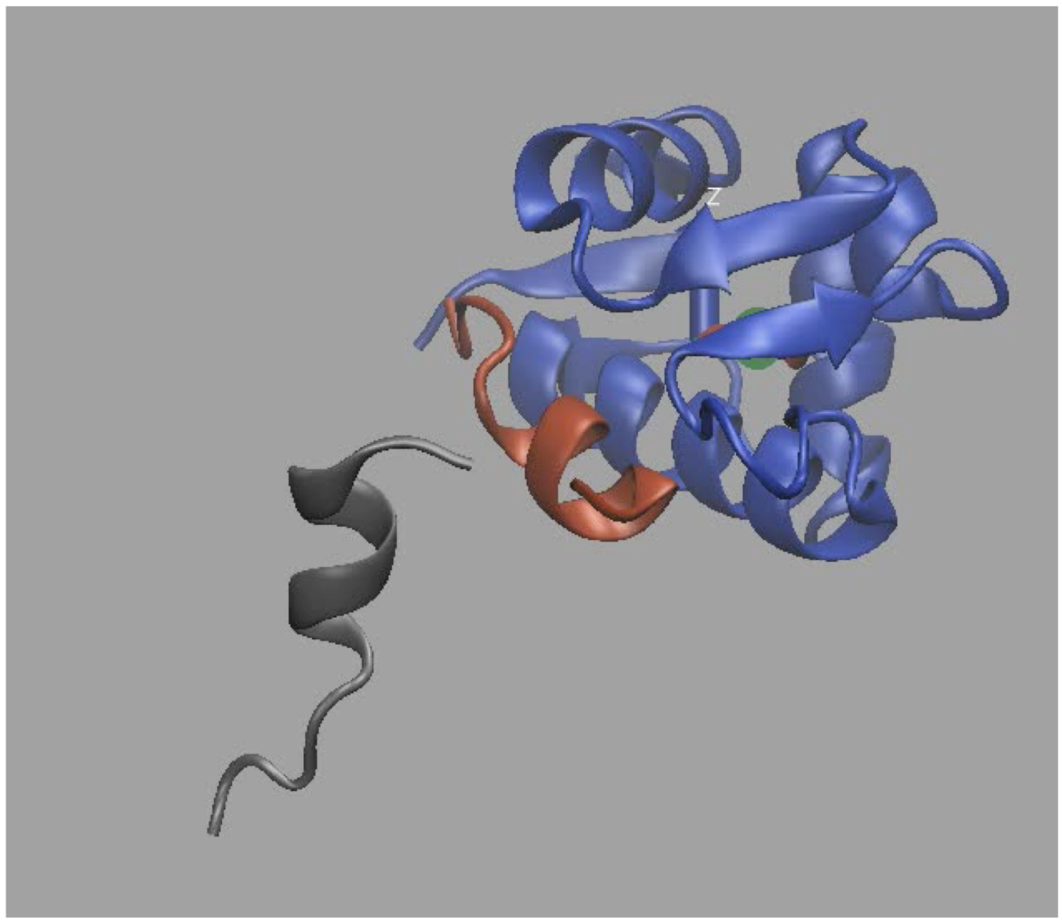
**Left:** VISM pockets (primary: red; secondary: blue; tertiary green; etc.)
**Right:** A primary pocket in a hydrophilic region aligned with a cocrystalized ligand.

# Martini-VISM: Barstar-barnase



| grid size (Å) | grid number | LSM: rel. error | B-LSM: rel. error | LSM: time | B-LSM: time (s) |
|---|---|---|---|---|---|
| 0.64 | $25 \times 25 \times 25$ | 0.0412 | 0.0298 | 1.10 | 0.01 |
| 0.32 | $50 \times 50 \times 50$ | 0.0124 | 0.0245 | 11.97 | 0.10 |
| 0.16 | $100 \times 100 \times 100$ | 0.0026 | 0.0136 | 186.44 | 1.41 |
| 0.08 | $200 \times 200 \times 200$ | 0.0015 | 0.0099 | 5032.03 | 26.11 |

Table 1. Comparison of the level-set method (LSM) and the fast binary level-set method (B-LSM).



# Thank You!