SPATIOTEMPORAL MODELING OF BACTERIAL CO-CULTURE USING PARTIAL DIFFERENTIAL EQUATIONS

Mohammad Taha Farooqui

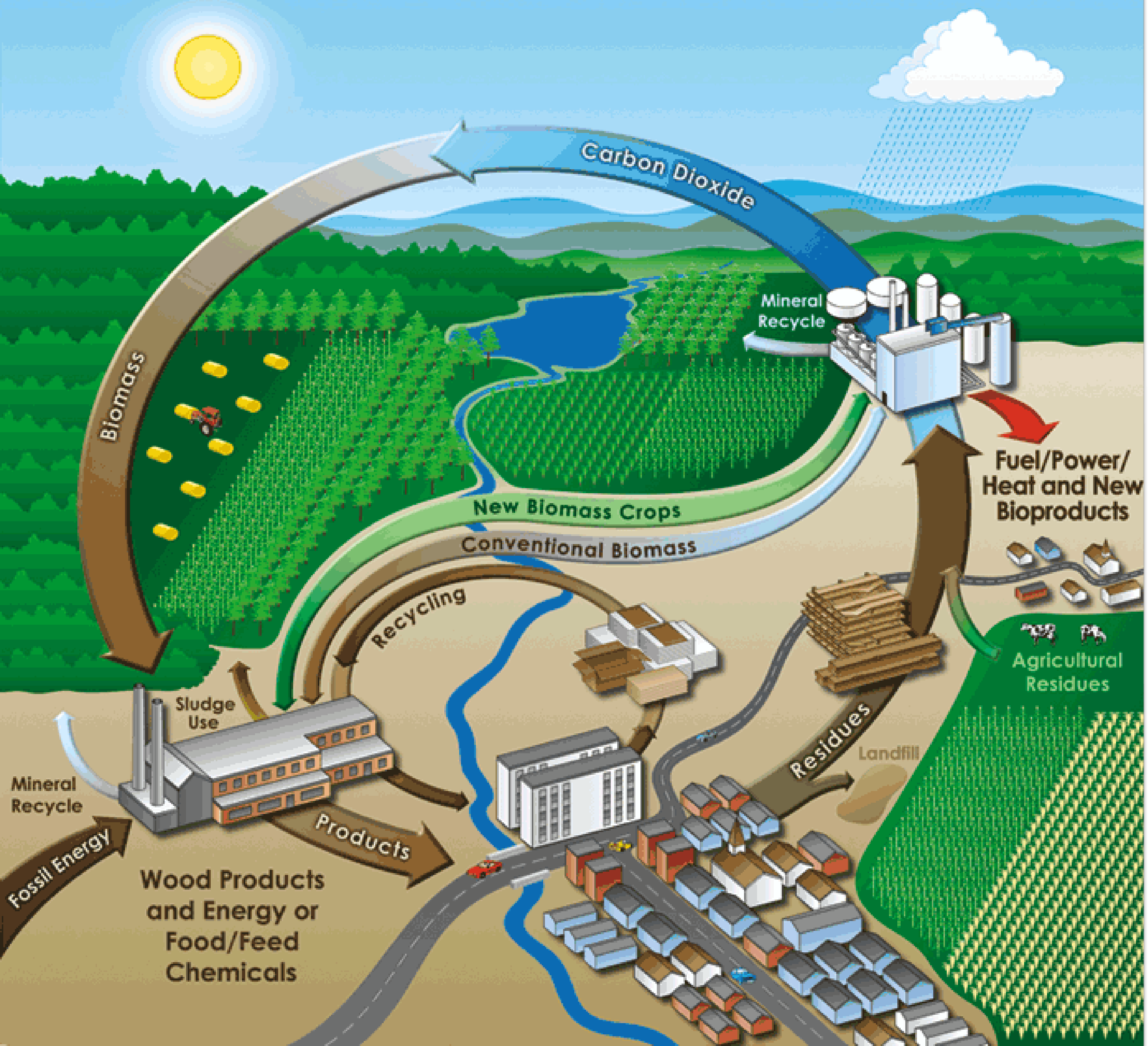
Supervisor: Brian Ingalls, Brenda Lee

University of Waterloo

PHYS 437A

GOAL OF THE PROJECT

- Incorporate experimental data on monoculture growth and parameter estimates into the model
- Use the model to investigate how the presence of a second bacterial strain affects the growth and spatial distribution of the first strain
- Compare the model predictions with experimental observations of co-cultured bacteria growing on agar pads
- Explore the impact of different growth conditions and initial conditions on the dynamics of the bacterial co-culture
- Develop a quantitative understanding of the factors that influence the spatial organization of bacterial co-cultures.

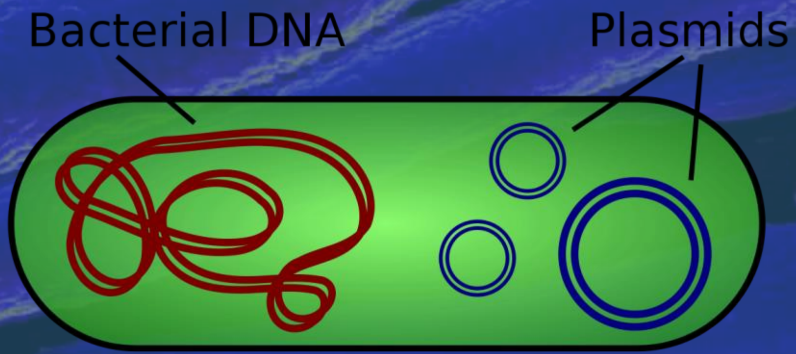


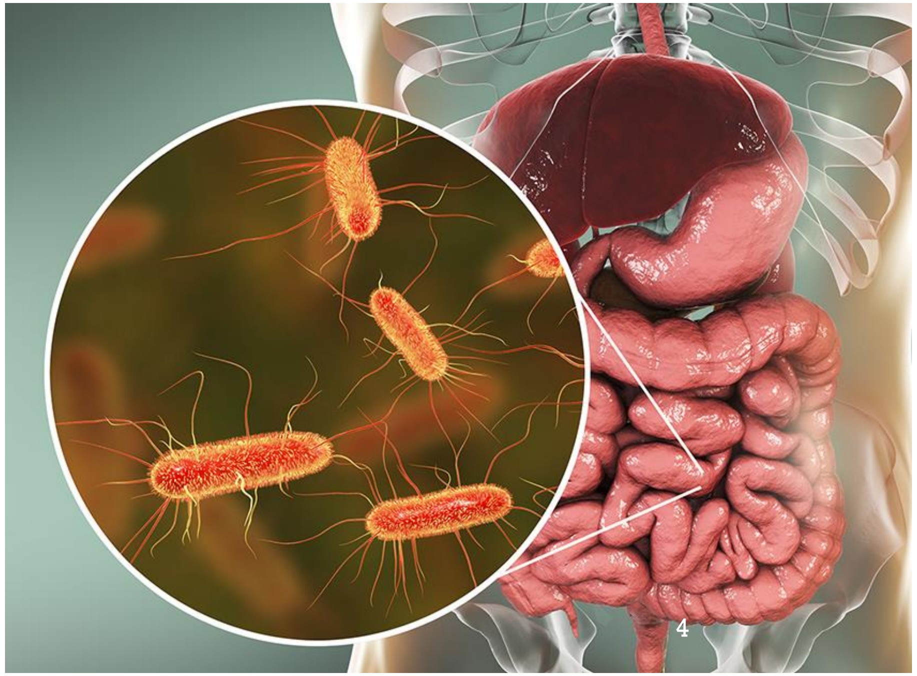
MOTIVATION

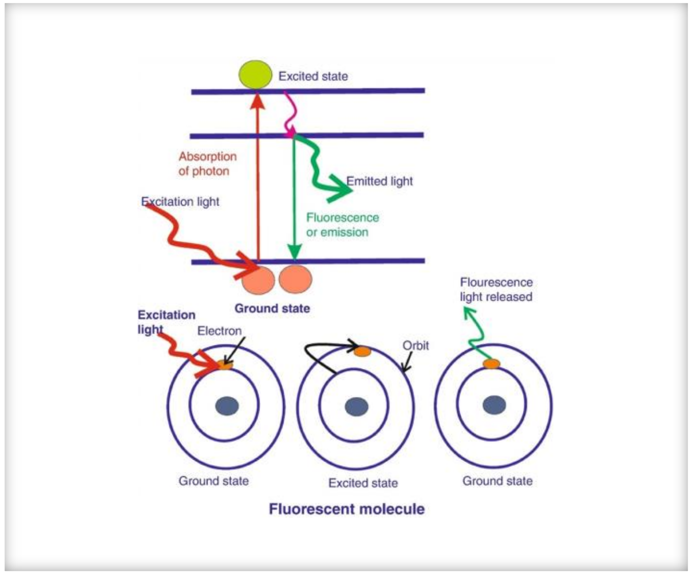
- Bioremediation
- Agriculture
- Biofuel
- Wastewater treatment
- Bioproduction (such as medicine, food, chemicals)

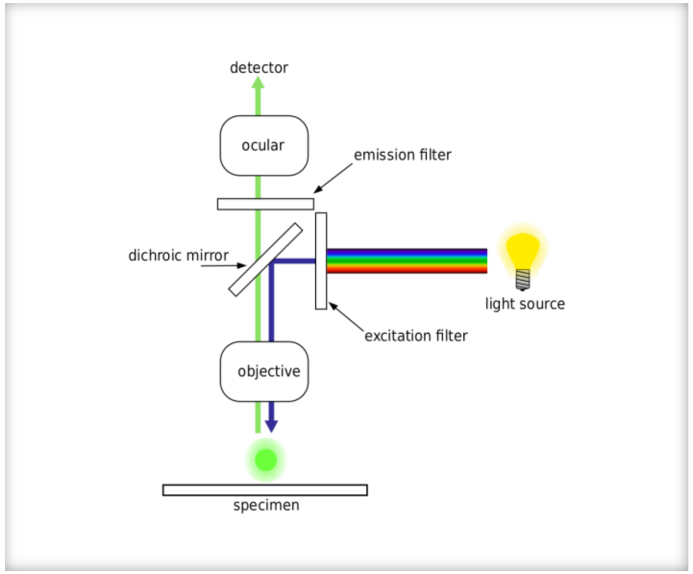
ESCHERICHIA COLI

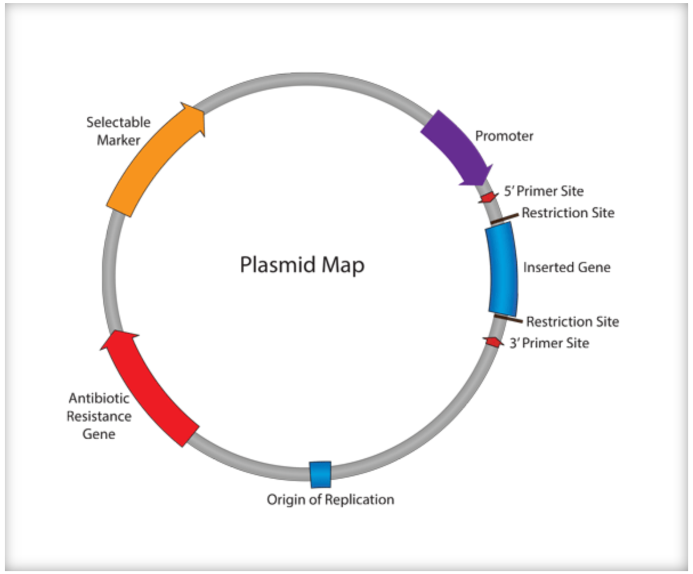
- A common Rod-shaped bacteria
- Fast growth rate
- Simple genetics
- Easy to engineer











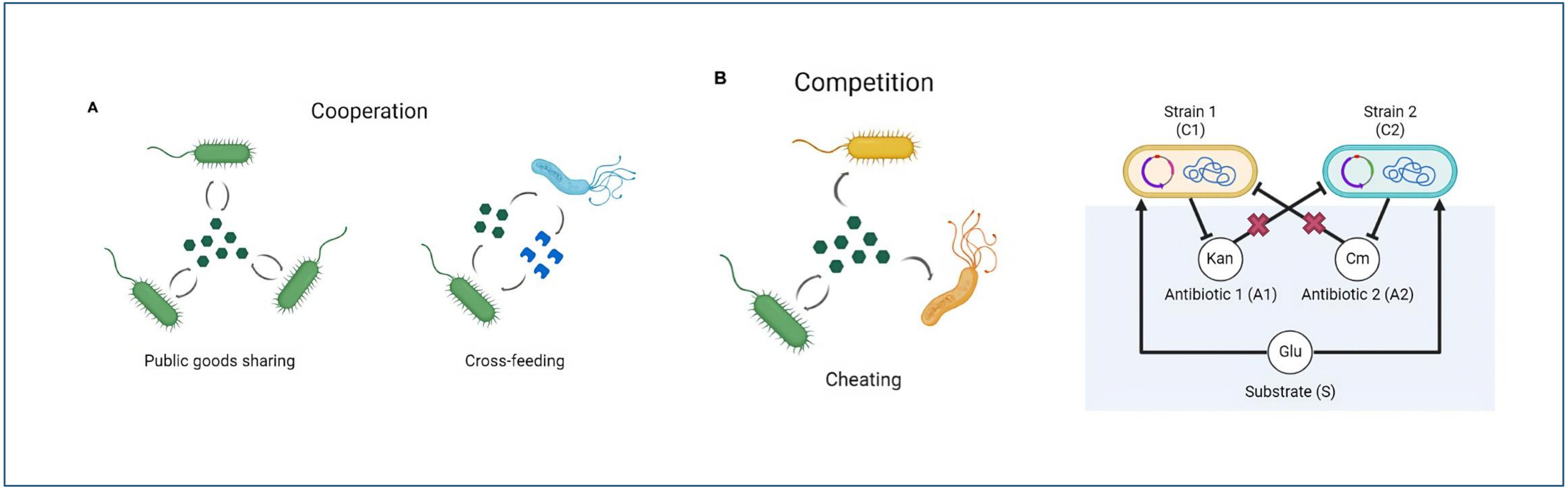
FLORESCENT MARKERS

ABSORB AND EMIT LIGHT

BIOLOGICAL LABELING

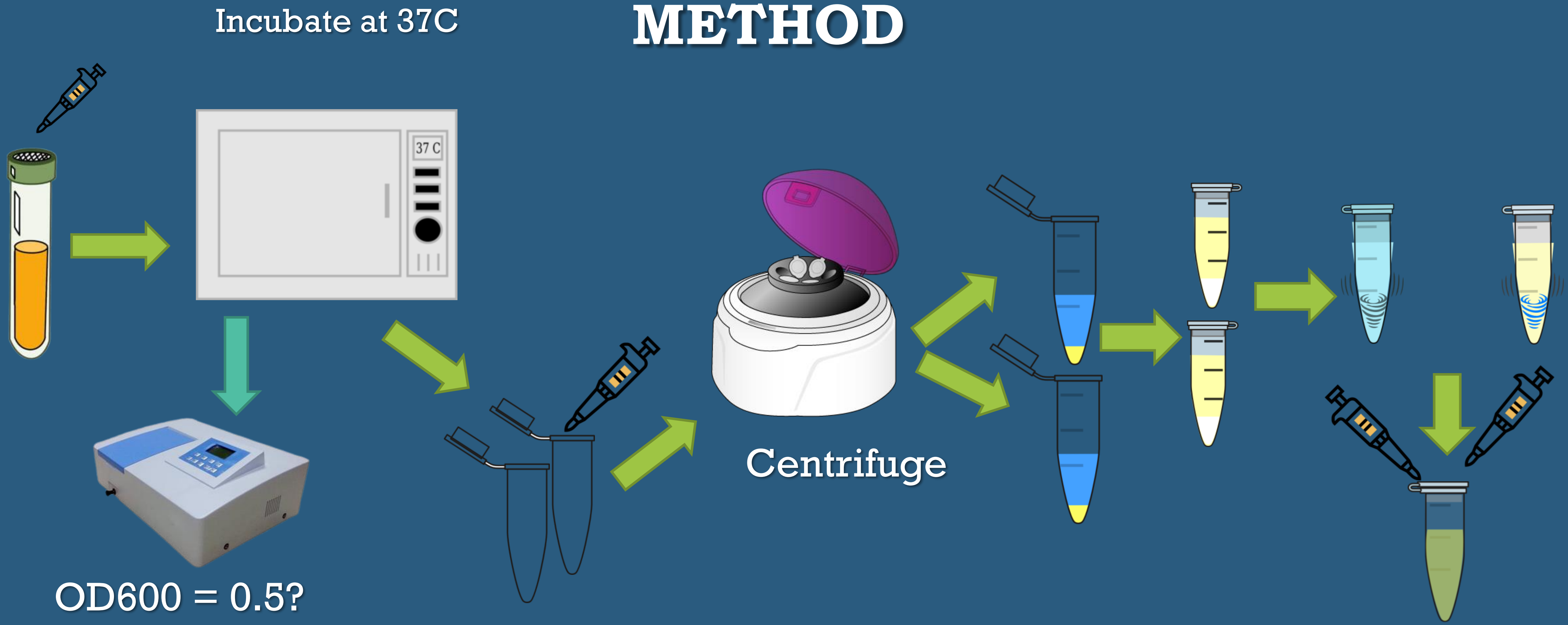
SPECIFIC TARGETS

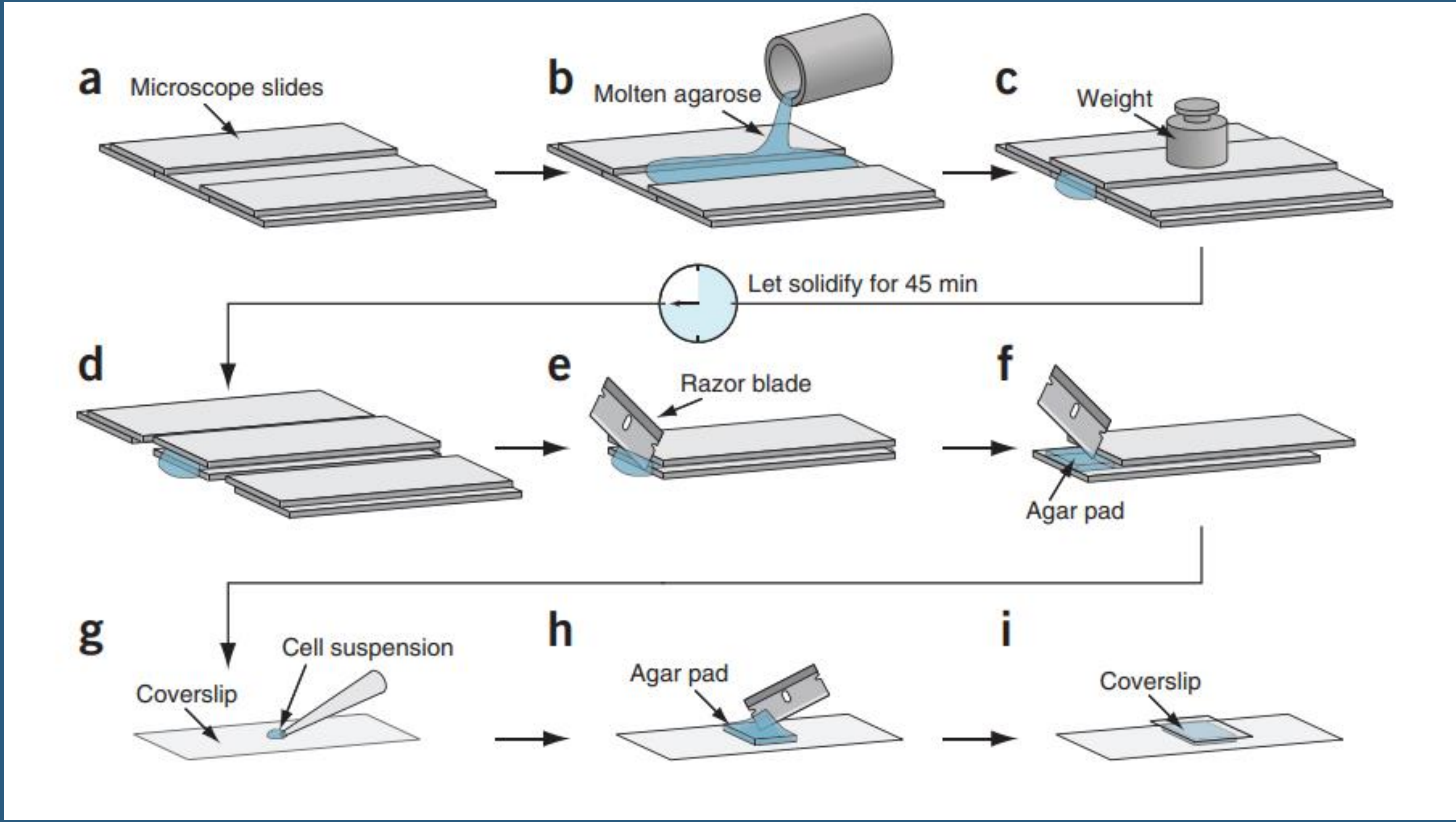
DYNAMIC IMAGING



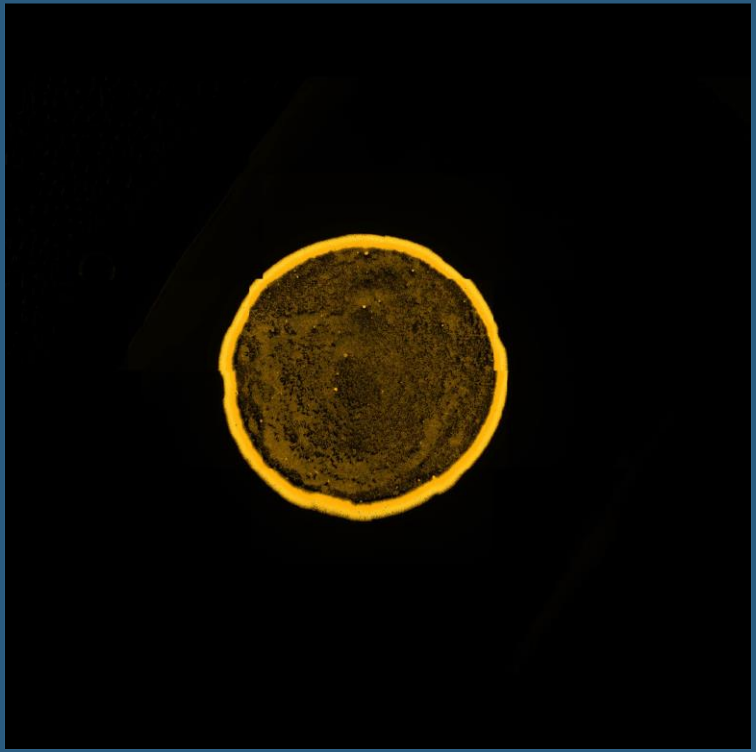
CHEATERS VS COOPERATORS

METHOD

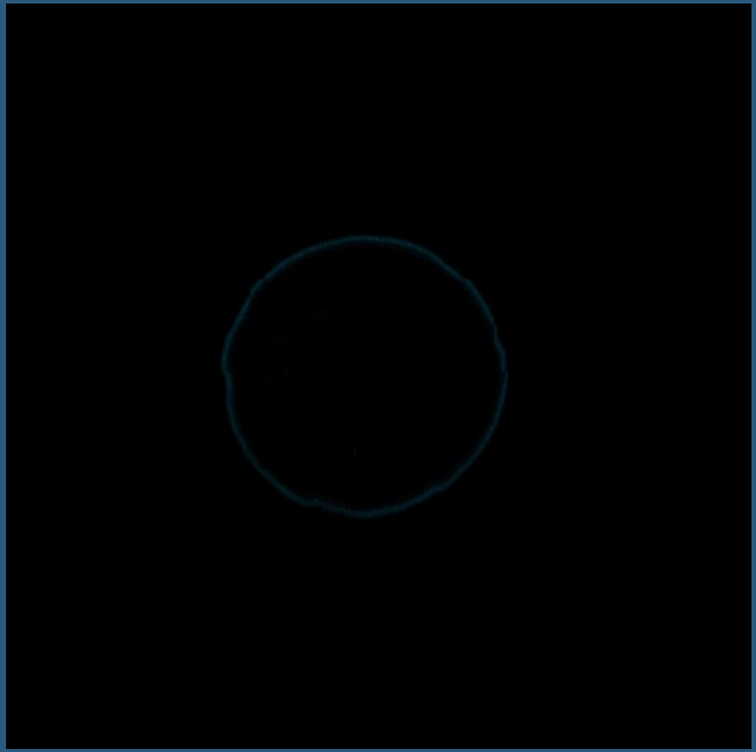



a
Microscope slides
b
Molten agarose
c
Weight
Let solidify for 45 min
d
e
Razor blade
f
Agar pad
g
Cell suspension
Coverslip
h
Agar pad
i
Coverslip

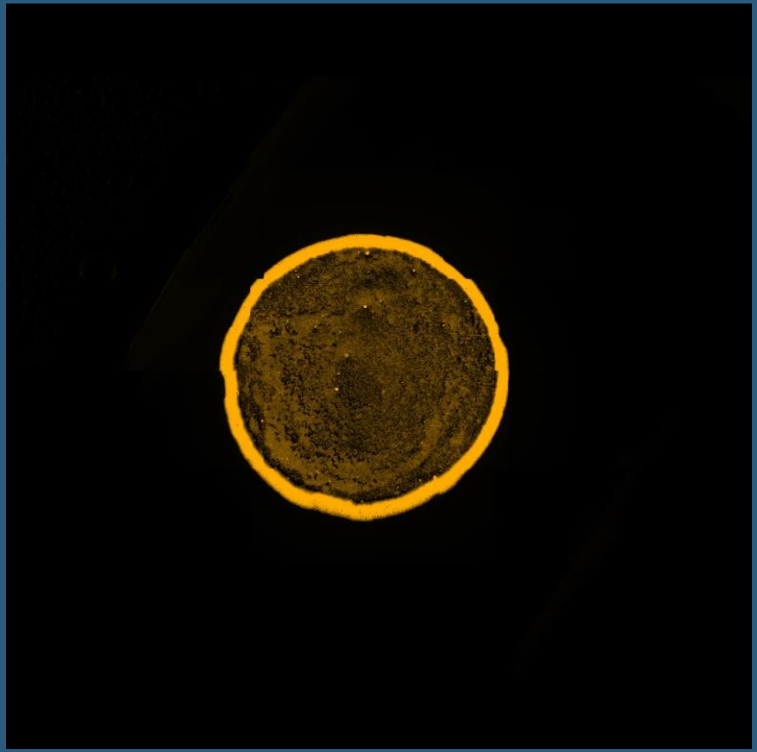
RESULTS



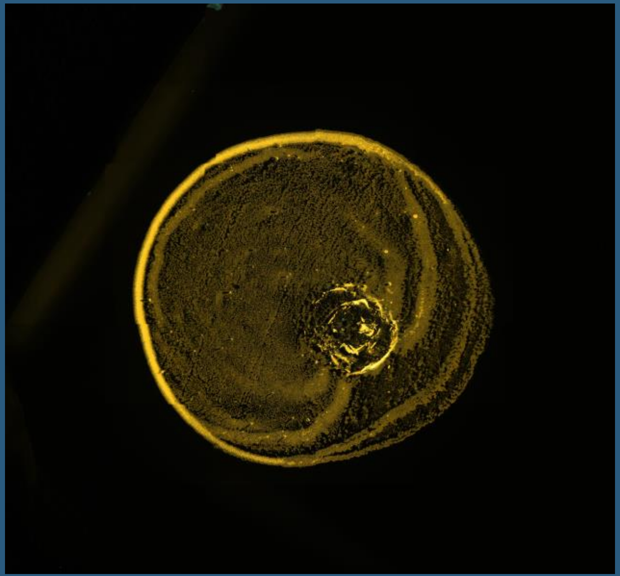
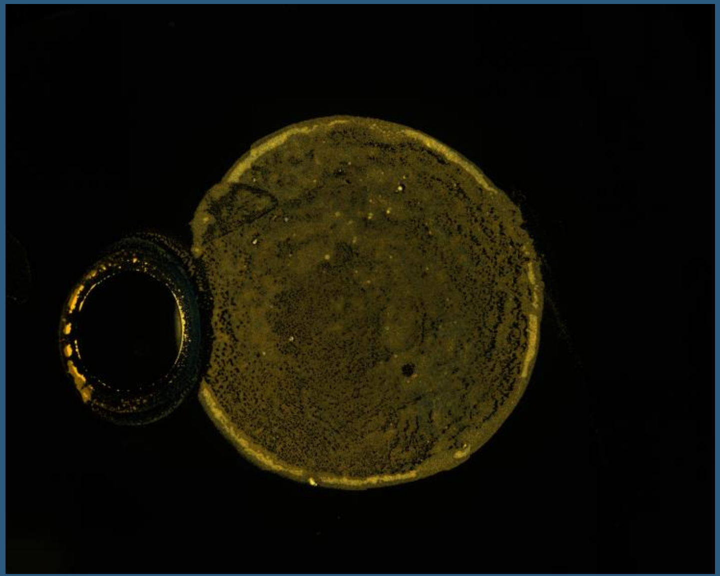
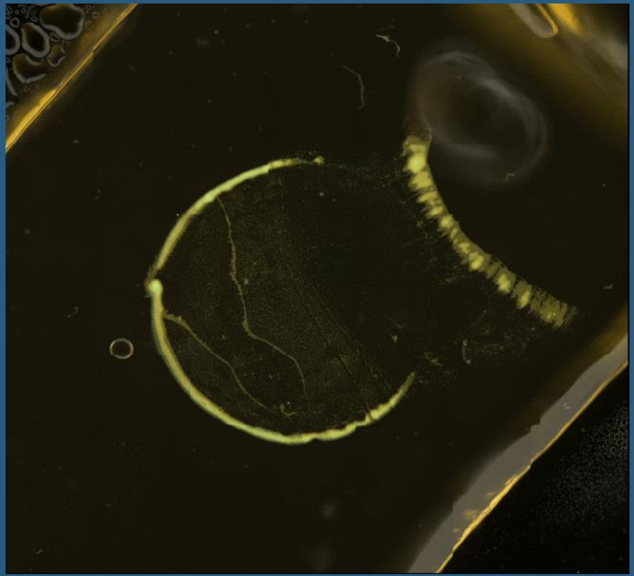
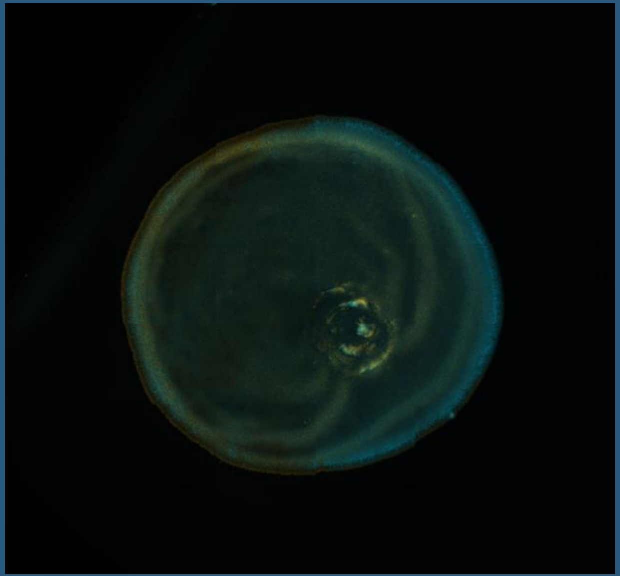
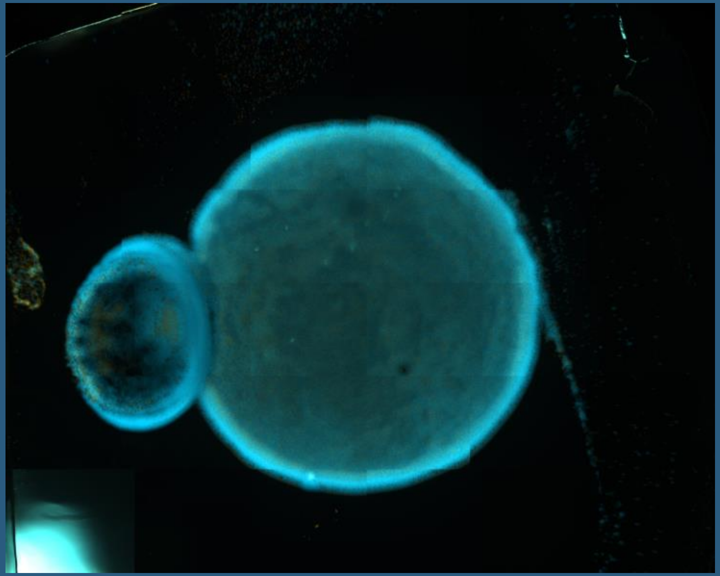
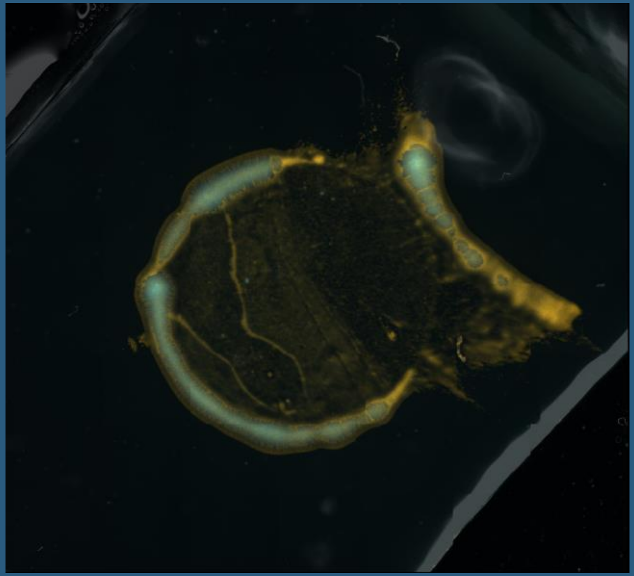
Time-lapse of CFP and Cy3 strains growing



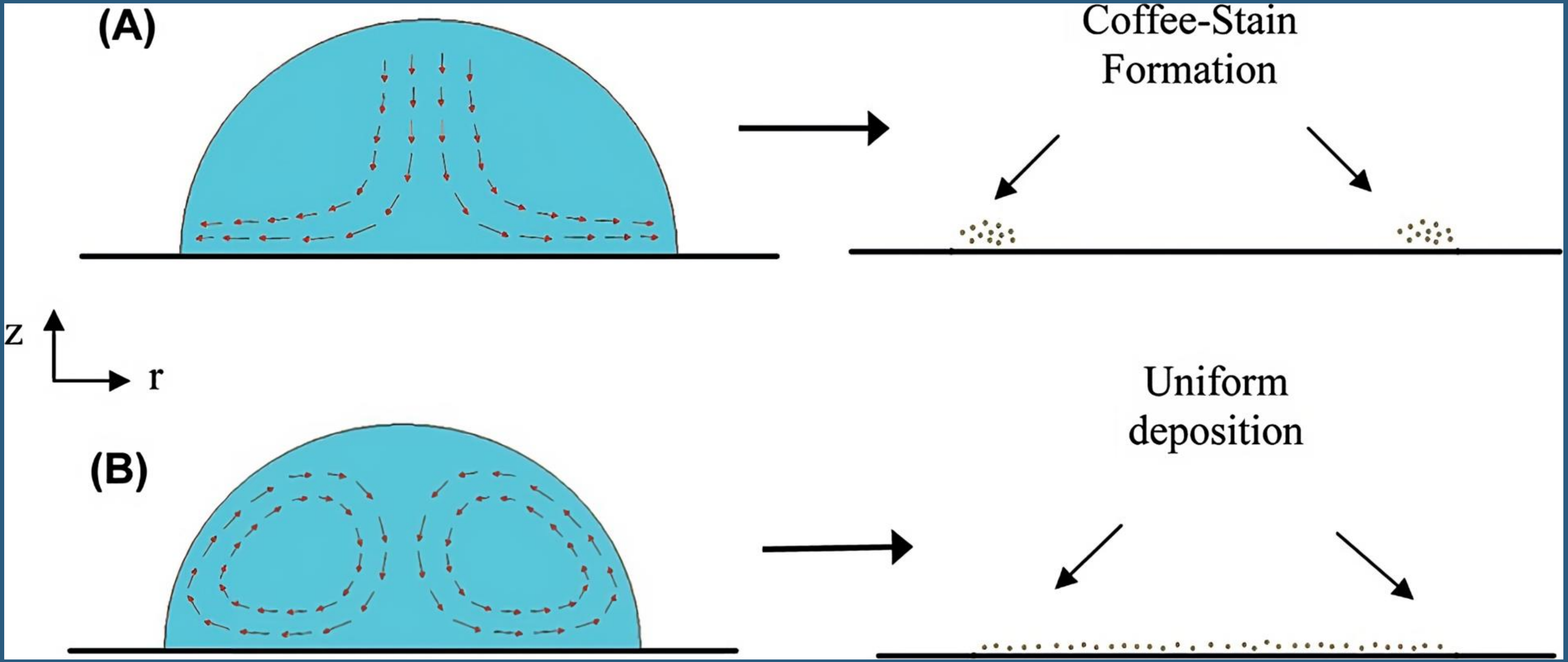
CFP isolated



Cy3 isolated

COFFEE-RING EFFECT



PDE MODELING

- $\frac{\partial C}{\partial \epsilon} = \alpha_0(D(C)\nabla c) + M$

$$D(C) = pq + C\left(p\frac{\partial q}{\partial C} - q\frac{\partial p}{\partial C}\right)$$

$$M = M_1 c_1 + M_2 c_2$$

$$M_1 = \mu_1\left(\frac{s}{\mathrm{K}_s + s}\right)\left(\frac{1}{1 + \left(\frac{A_2}{IC_{50,2}}\right)^{n_2}}\right)$$

$$M_2 = \mu_2\left(\frac{s}{\mathrm{K}_s + s}\right)\left(\frac{1}{1 + \left(\frac{A_1}{IC_{50,1}}\right)^{n_1}}\right)$$

M: Reaction term, related to growth rate

p and q are density dependent dispersal terms

c_1 and c_2 are cell densities of the 2 strains

A_1: Kanamycin concentration (antibiotic 1)
A_2: Chloramphenicol concentration (Antibiotic 2)
IC_{50}: Half response for either antibiotic

K_s: reaction kinetic constant for uptake of glucose

n_1 and n_2 related to steepness of Km and Cm responsive curves

PDE MODELING

$$\frac{\partial C}{\partial t} = \alpha_0\left(p\nabla_2\left(C_q\right) - Cq\nabla^2 p\right) + M$$

$$\frac{\partial C}{\partial t} = \delta_0(p\nabla^2(Mq) - Mq\nabla^2 p) + Mp$$

$$\frac{\partial c_1}{\partial t} = \delta_0\left(p\nabla^2 \frac{Mqc_1}{c_1 + c_2} - \frac{Mqc_2}{c_1 + c_2}\nabla^2 p\right) + M_1 c_1 p$$

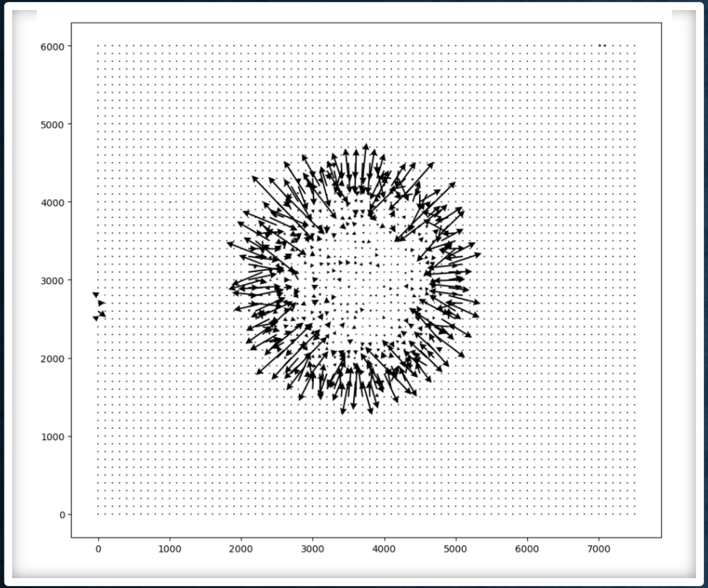
$$\frac{\partial c_2}{\partial t} = \delta_0\left(p\nabla^2 \frac{Mqc_2}{c_1 + c_2} - \frac{Mqc_2}{c_1 + c_2}\nabla^2 p\right) + M_2 c_2 p$$

δ_0: Dispersal constant
δ_{A_1}: Diffusion constant for Km
δ_{A_2}: Diffusion constant for Cm

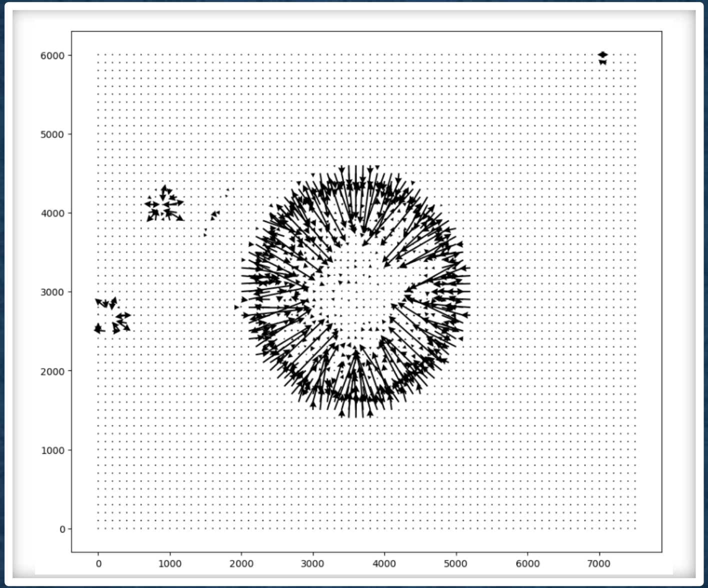
$$\frac{\partial s}{\partial t} = \delta_s \nabla^2 S - \frac{M}{Y}$$

$$\frac{\partial A_1}{\partial t} = \delta_{A_1}\nabla^2 A_1 - V_{\max,1}\frac{A_1 c_1}{k_{m,1} + A_1}$$

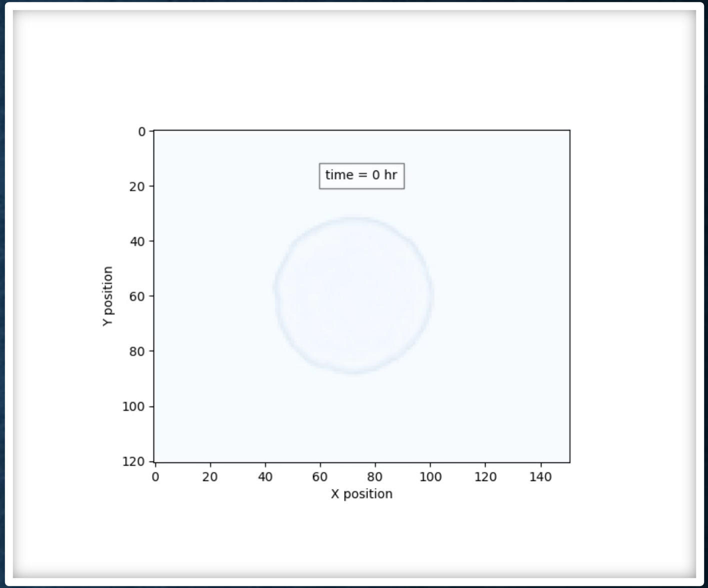
$$\frac{\partial A_2}{\partial t} = \delta_{A_2}\nabla^2 A_2 - V_{\max,2}\frac{A_2 c_2}{k_{m,2} + A_2}$$



Initial vector field of CFP at t=0

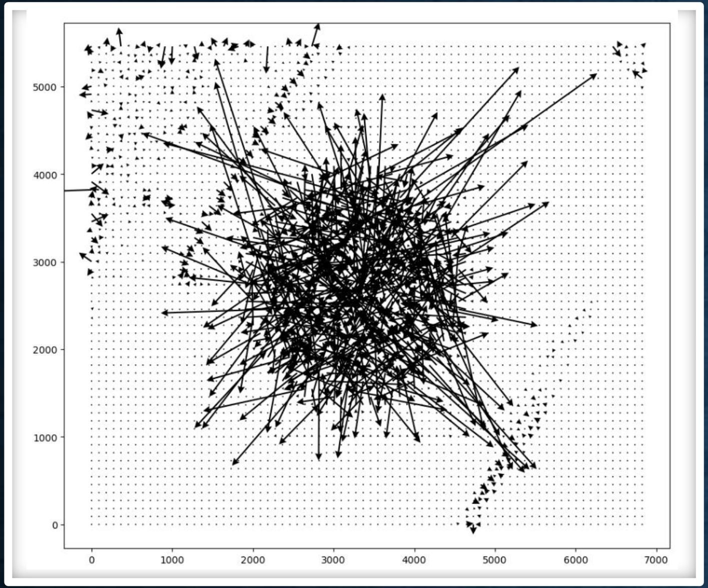


Vector field of CFP at t=24h

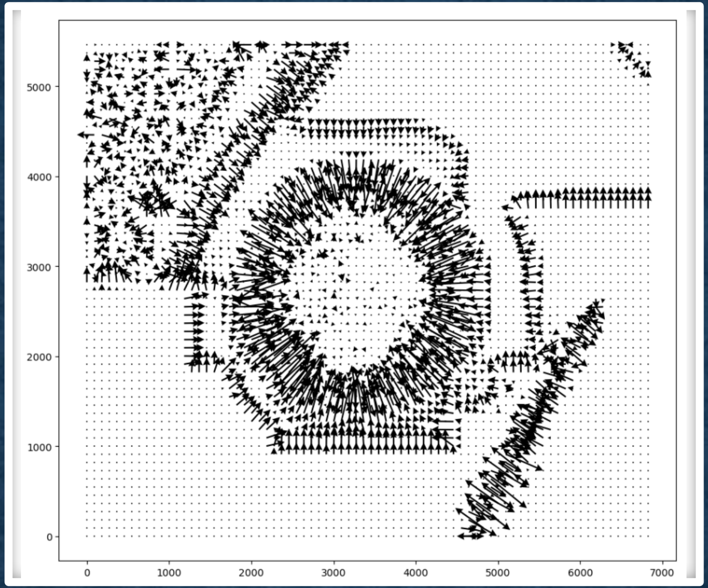


Simulation Timelapse

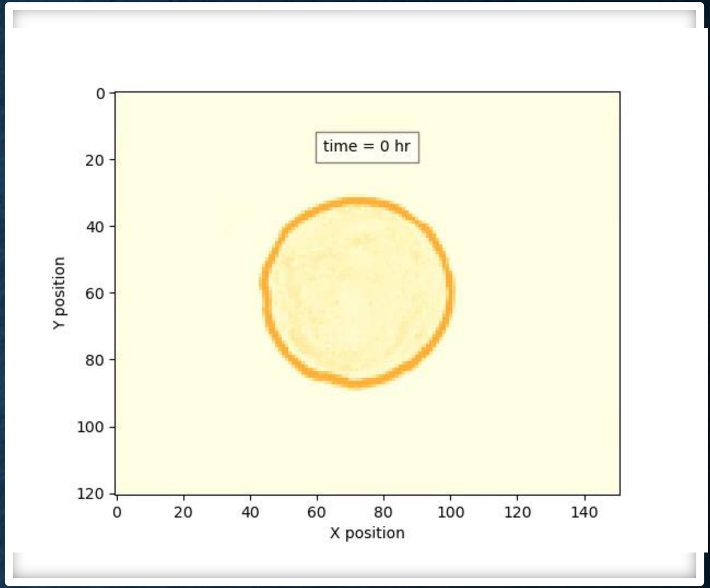
SIMULATIONS



Initial vector field
of Cy3 at t=0



Vector field of
Cy3 at t=24h



Simulation
Timelapse

SIMULATIONS

LIMITATIONS AND FUTURE WORK

- Model predicts the experimental data
- Parameters estimation through model is a long process

- Enzyme kinetics experiments to determine parameters more accurately