# MUTATIONS AND MOTILITY

CHRIS GUIVER, JAMES HORTON, YYANIS JOHNSON-LLAMBIAS, DAN NG, NICK PRIEST, CAMERON SMITH, JOSH YOUNG

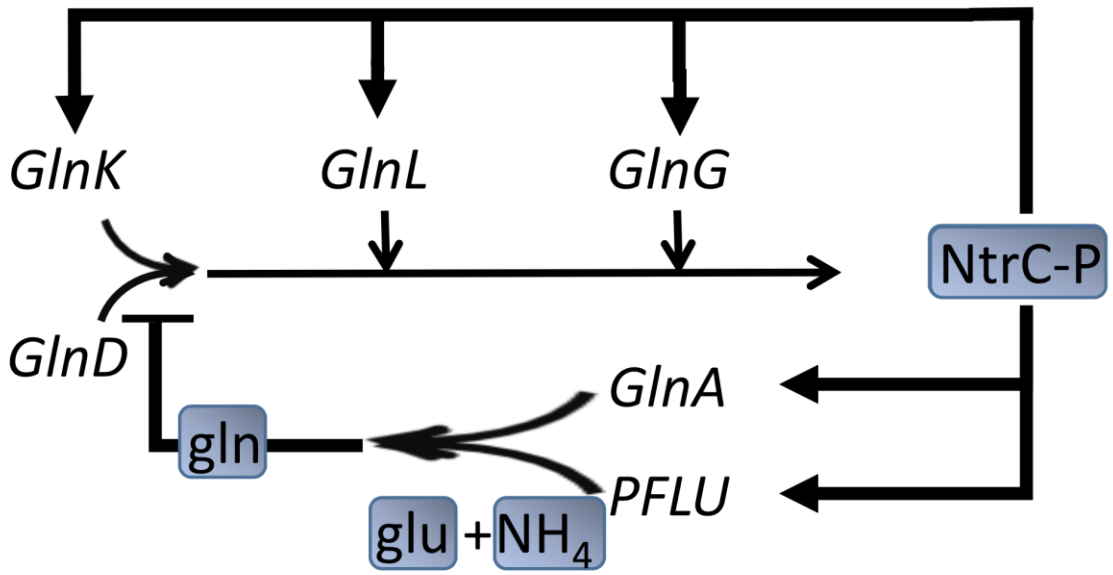
# THE PROBLEM

The problem:

- Random mutations occur in genes that encode proteins.
- Certain mutations can cause cells to become motile.
- Can be dangerous (can lead to cancer metastasis etc.).

Our Aim:

- What is the likelihood of any given gene achieving a mutation which turns on motility?



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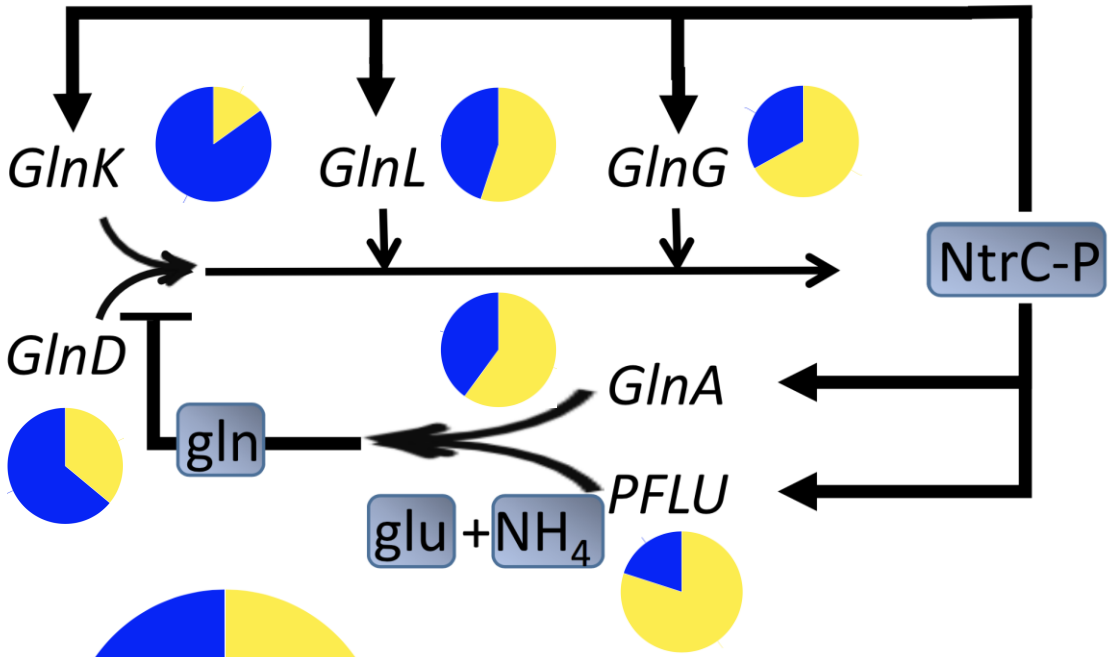
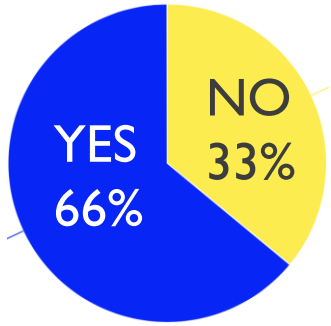
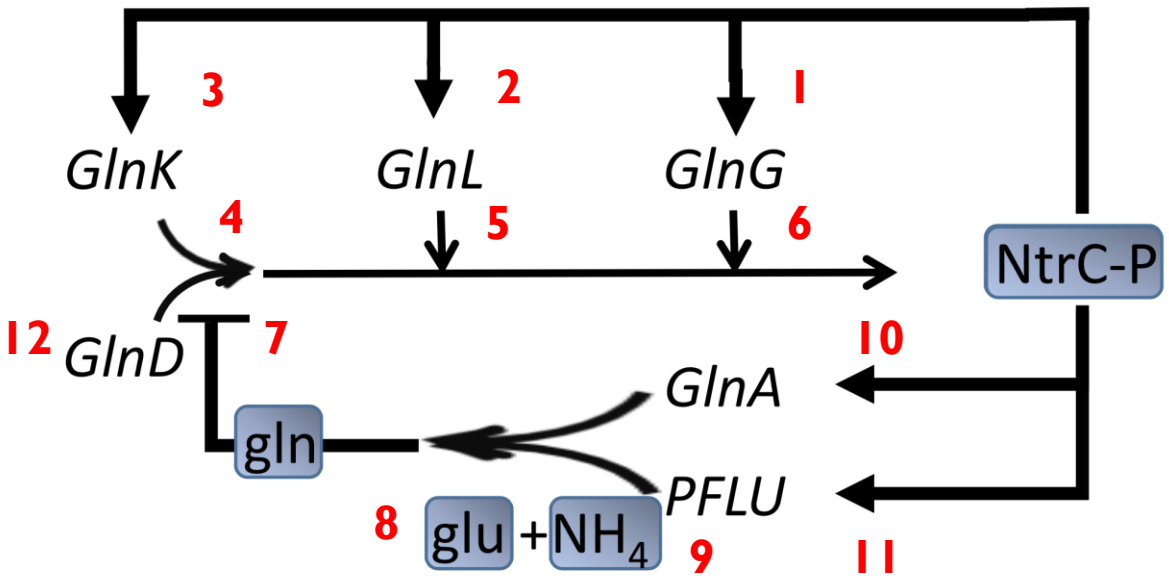



Will mutation lead to motility?

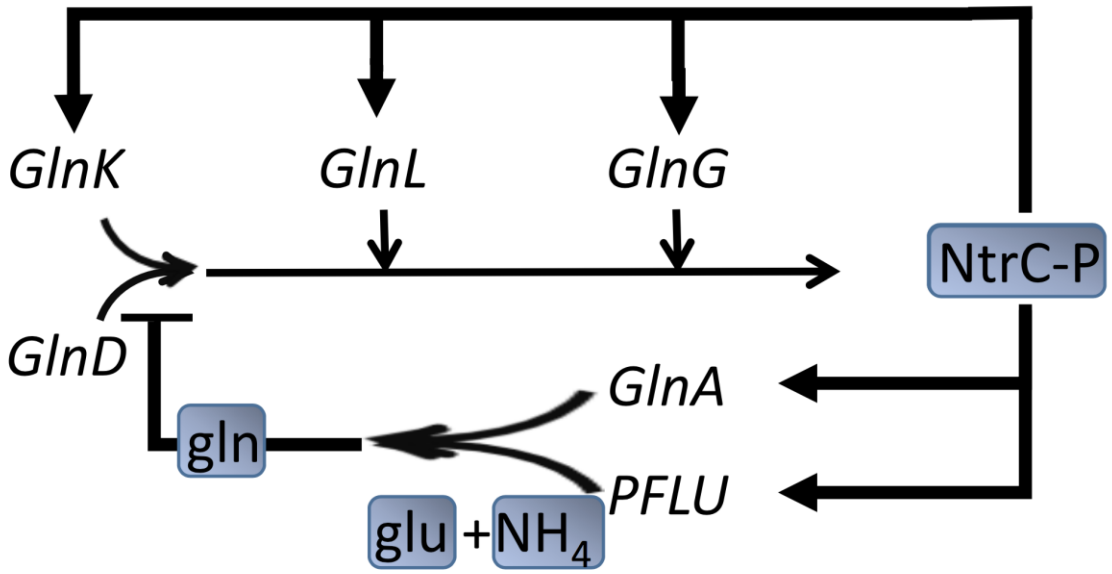
# ODE MODEL

| | | | |
|---|---|---|---|
| 1 | NtrC-P | → | NtrC-P + GlnG |
| 2 | NtrC-P | → | NtrC-P + GlnL |
| 3 | NtrC-P | → | NtrC-P + GlnK |
| 4 | GlnD + GlnK | → | C1 |
| 5 | C1 + GlnL | → | C2 |
| 6 | C2 + GlnG | → | NtrC-P |
| 7 | gln + GlnD | → | ∅ |
| 8 | glu+ $NH_4$+ GlnA | → | gln + GlnA |
| 9 | PFLU | → | glu + $NH_4$ + PFLU |
| 10 | NtrC-P | → | GlnA + NtrC-P |
| 11 | NtrC-P | → | PFLU + NtrC-P |
| 12 | ∅ | → | GlnD |



# MODELLING ASSUMPTIONS

- Direct reactions from NtrC-P modelled using Michelis-Mentin, other reactions modelled using law of mass-action.
- All Stoichiometric numbers in reactions are 1.
- No environmental changes/effects.
- Amount of gene is a proxy for gene expression.

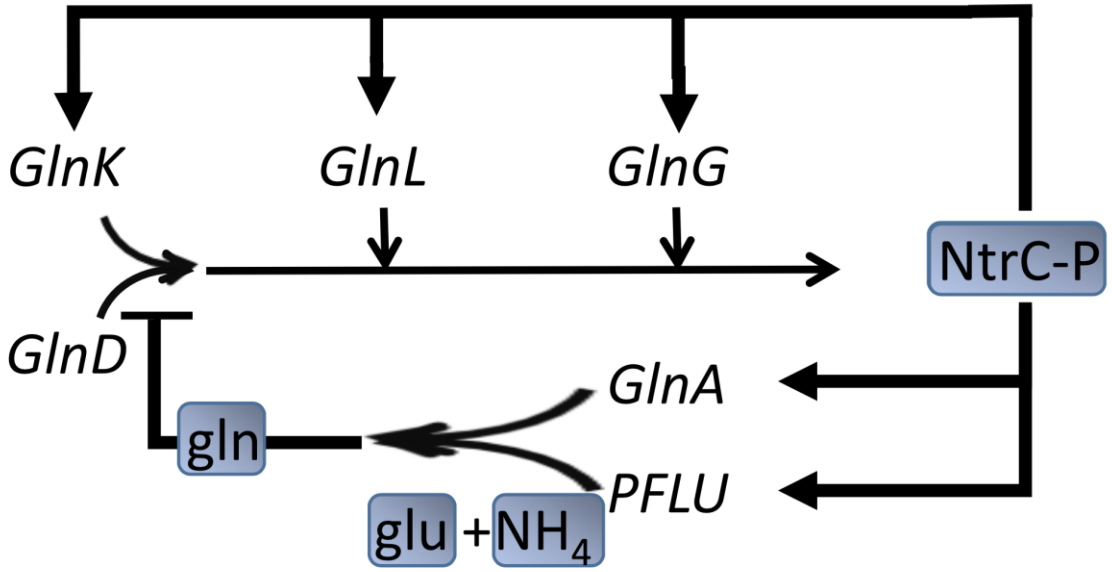


# ODE MODEL

*Following Rau et al. (2014), reaction dynamics are modelled by the system*

$$\dot{x} = \mathrm{Z}\mathrm{B}v(x) + \mathrm{Z}v_b(x),$$

- $\mathrm{Z}$ is the *complex stoichiometric matrix.*
- $\mathrm{B}$ is the *incidence matrix.*
- $v(x)$ is vector of reaction rates.
- $\mathrm{Z}v_b(x)$ is term modelling environmental inputs (flux of substrate etc.). We will ignore for now.



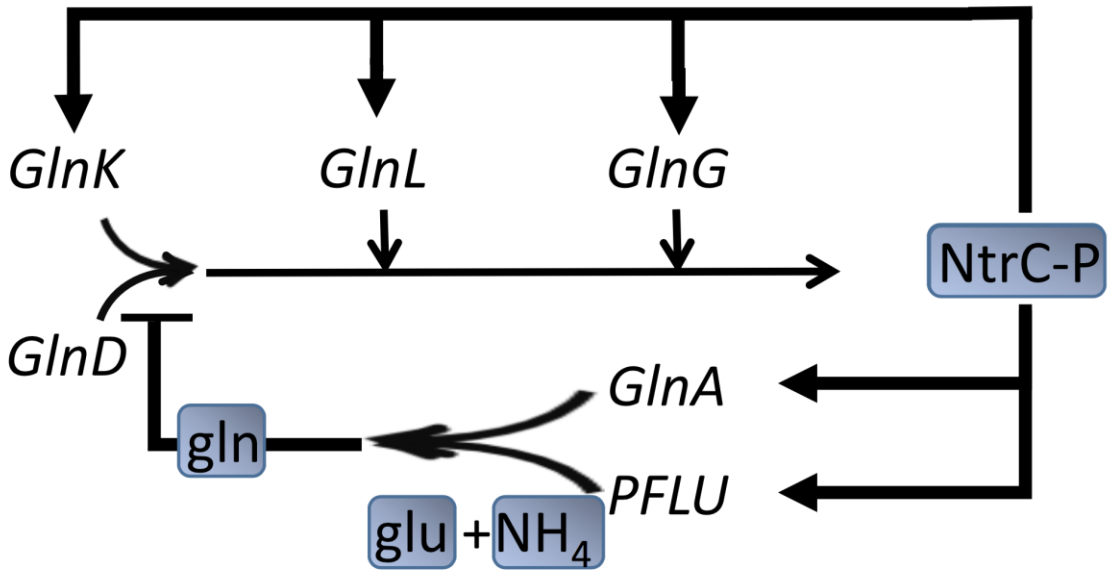
# STEADY STATES BEFORE AND AFTER MUTATION

Consider mutation which removes need for GlnK + GlnD complex in production.

For steady state, solve

$$0 = \mathrm{ZB}v(x).$$

- Employ Newton-type solver in MATLAB (e.g. fsolve).



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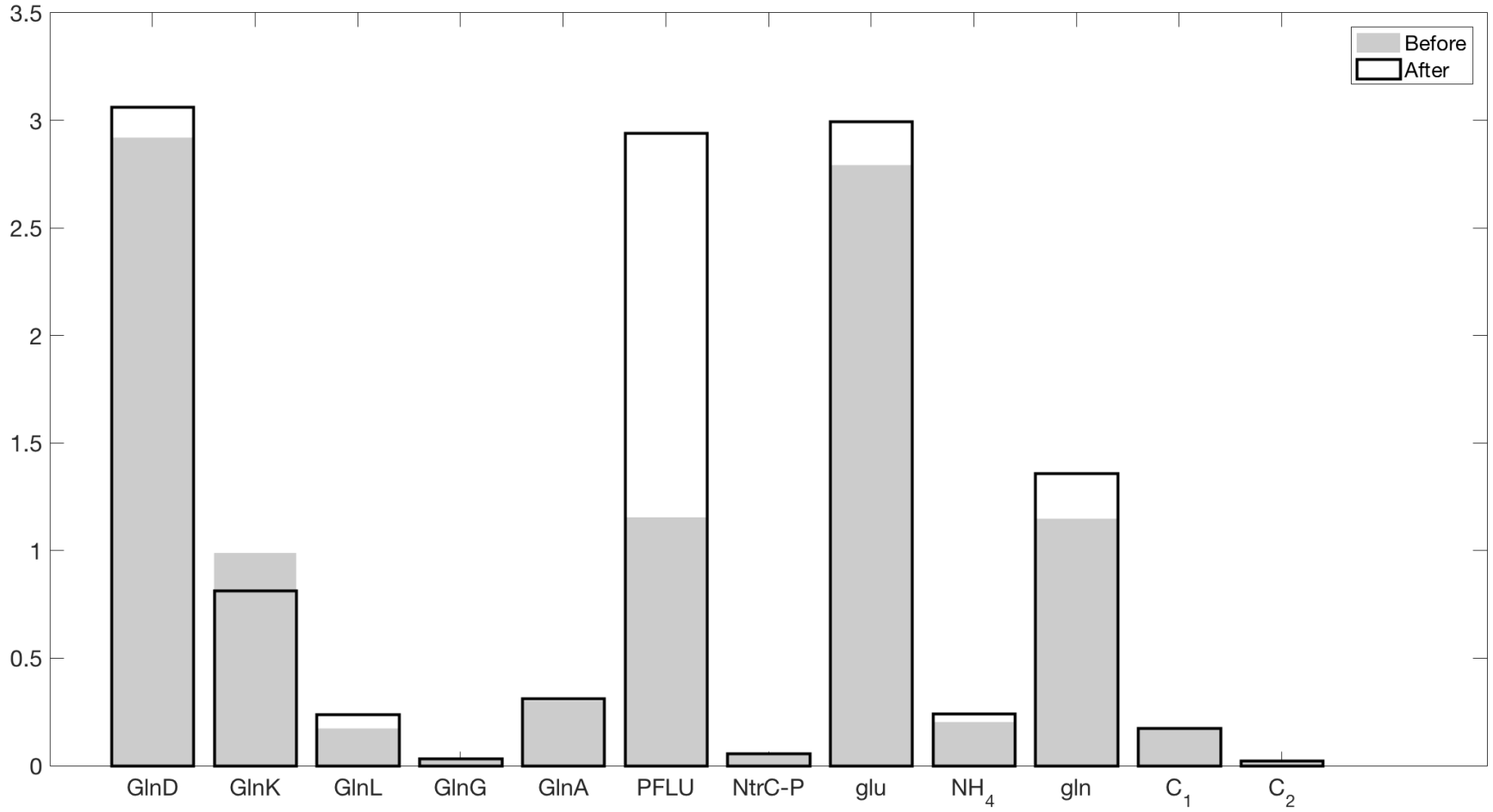
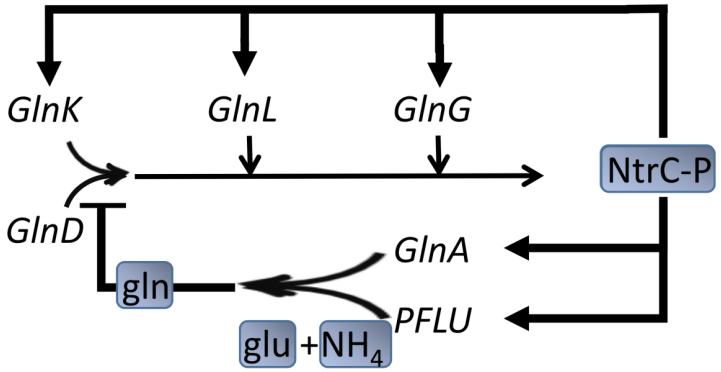


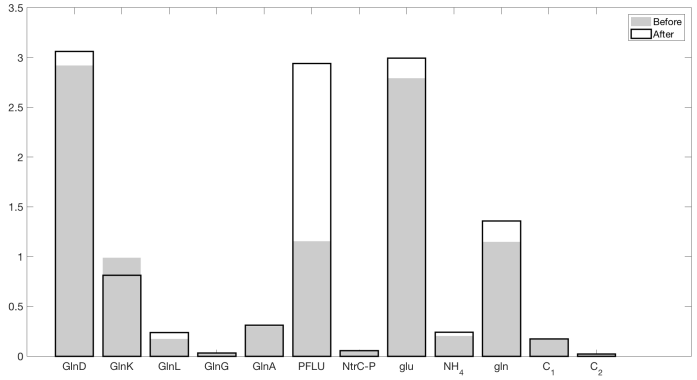
# WHY ISN'T STEADY STATES APPROACH IDEAL?

For steady state, solve

$$0 = \mathrm{ZB}v(x).$$

- Employ Newton-type solver in MATLAB (e.g. fsolve).
- fsolvepicks up nearest zero to our initial guess… Not necessarily the one we want.
- Biological stability not the same as mathematical stability.
- Spike in NtrC-P production is not necessarily a stable process.



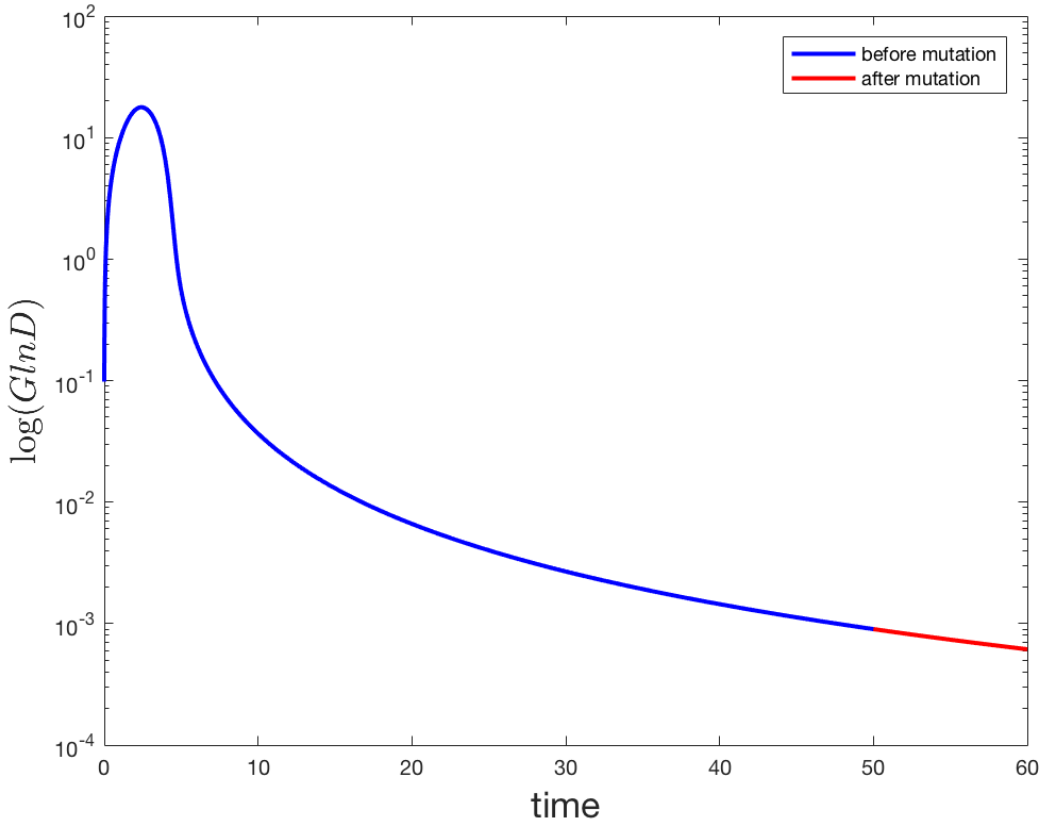
# SOLVING DYNAMICAL MODEL

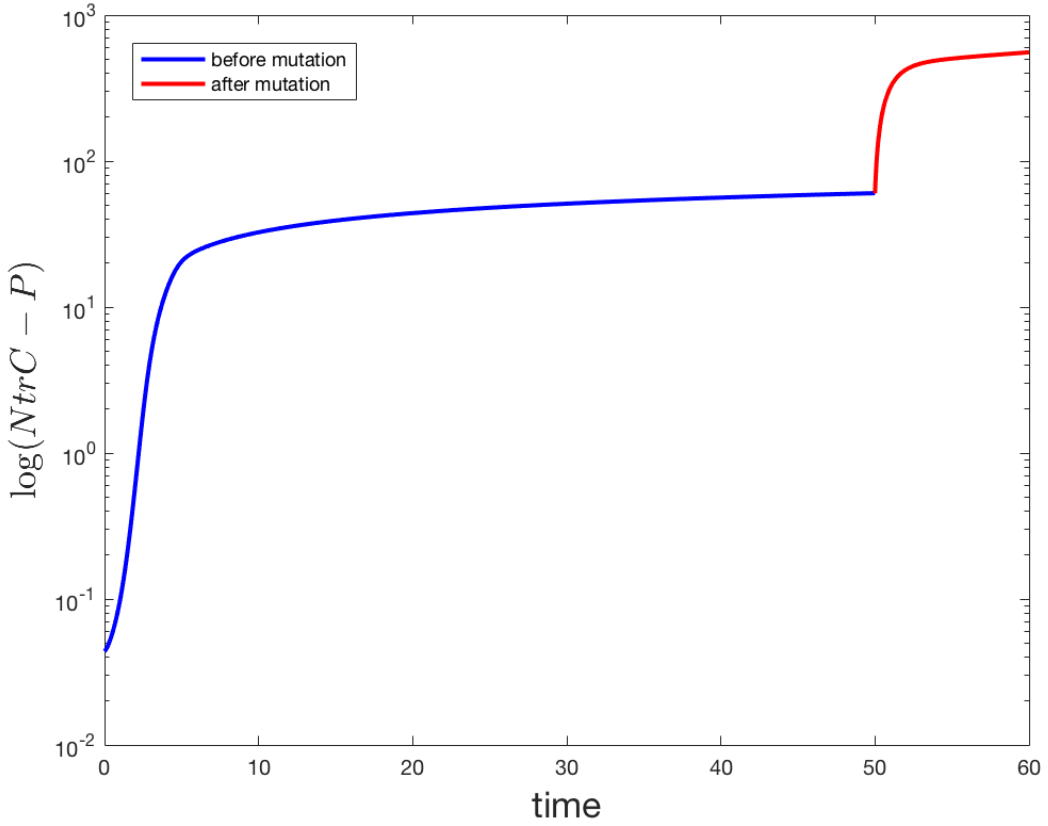
Instead, solve the dynamical system

$$\dot{x} = \mathrm{ZB}v(x)$$

- Employ some MATLAB ODE solver (ODE15 etc).

# GROWTH FROM MUTATION



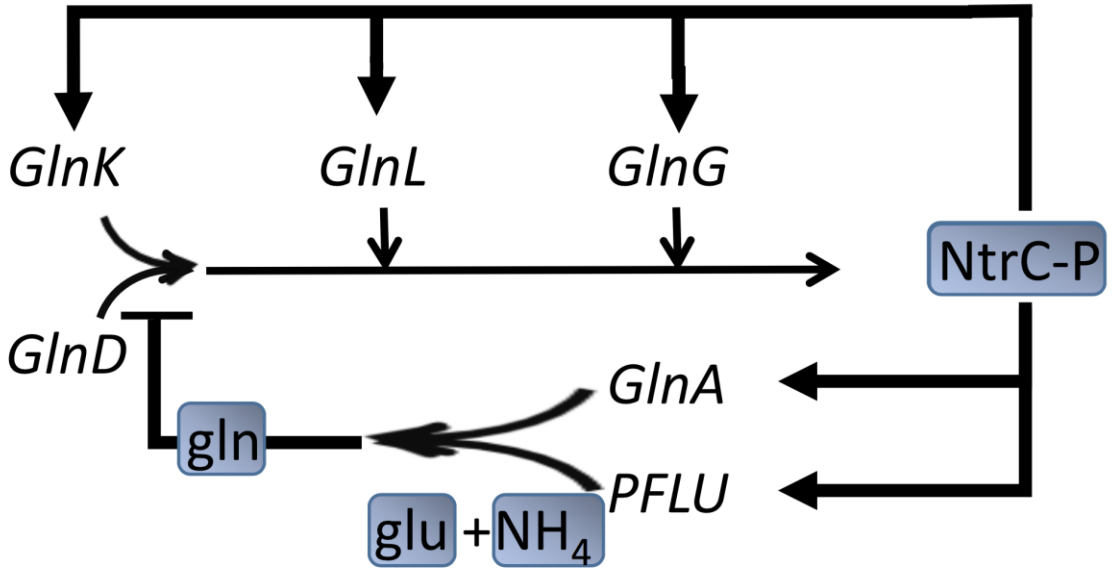



# POSSIBLE EXTENSIONS

- Following Rau et al. (2014), include environmental factors with $\mathrm{Z}v_b(x)$ term on the RHS of ODE

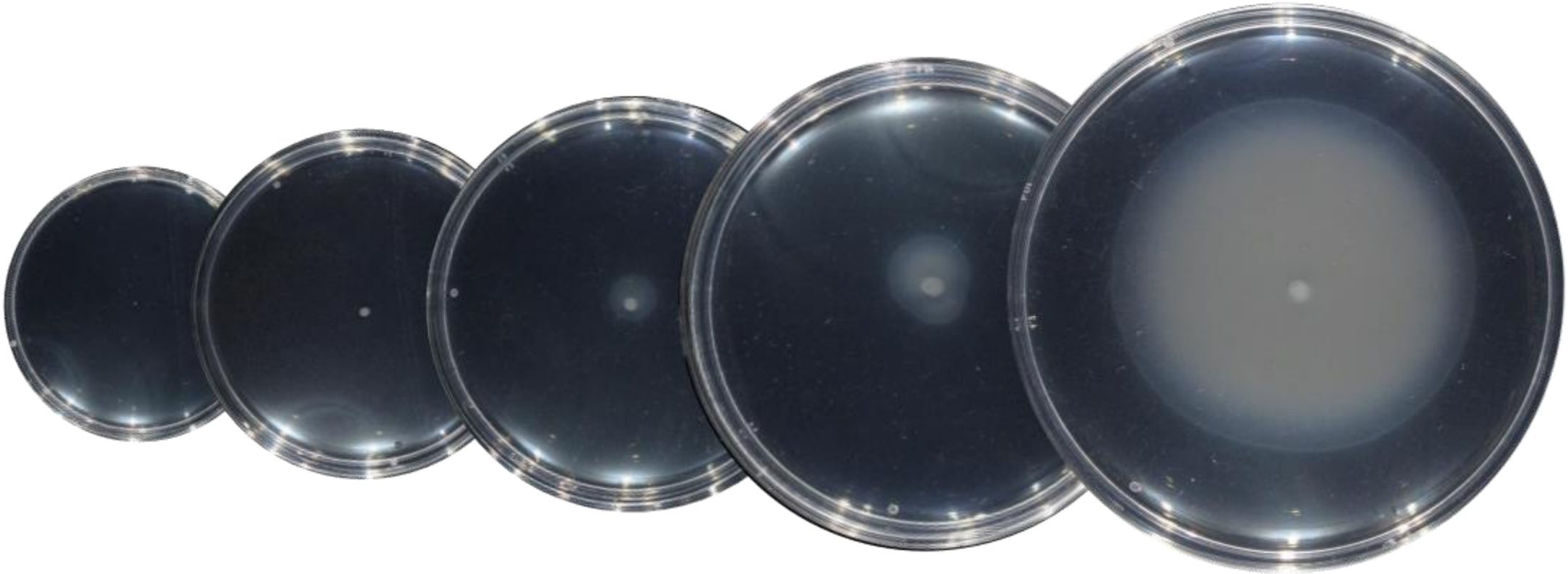
$$\dot{x} = \mathrm{ZB}(x)v(x) + \mathrm{Z}v_b(x).$$

- This can model fluxes of
- Explore different mutations. Do these mutations lead to higher NtrC-P?



# AGENT-BASED MODELLING

- Want to model the proliferation and mutation of the bacteria in the petri dish.



# THE MODEL

Submitted to Bulletin of Mathematical Biology

## Travelling waves in hybrid chemotaxis models

Benjamin Franz · Chuan Xue · Kevin J. Painter · Radek Erban

# THE MODEL – VELOCITY JUMP PROCESS

- Choose $\theta \sim \mathrm{Unif}(0, 2\pi)$ and jump a distance $v\Delta t$ in that direction, i.e.

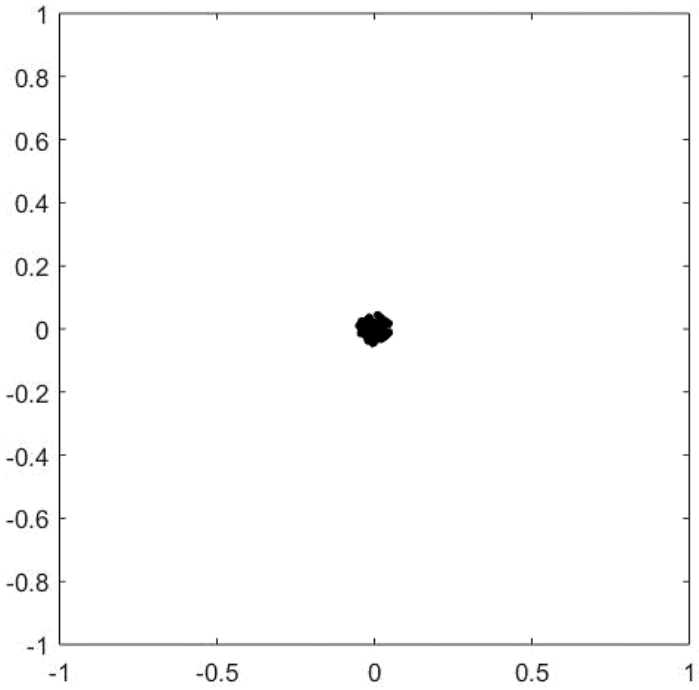
$$X_i(t + \Delta t) = X_i(t) + v\Delta t \begin{pmatrix} \cos(\theta) \\ \sin(\theta) \end{pmatrix}.$$

# THE MODEL - MUTATIONS

- The mutations are done through a series of reactions. Let $I, S, F$ denote the immobile, slow and fast moving bacteria. Then:

$$I \to 2I,$$
$$I \to I + S,$$
$$S \to 2S,$$
$$S \to S + F,$$
$$F \to 2F.$$

# THE RESULTS



# FUTURE STEPS

- Add the hybridisation from Franz *et al.* (2013):

$$S(x,t) = -\alpha_I \sum_{i=1}^{N_I} \delta\big(x - I_i(t)\big) - \alpha_S \sum_{j=1}^{N_S} \delta\left(x - S_j(t)\right) - \alpha_F \sum_{k=1}^{N_F} \delta\big(x - F_k(t)\big)\,.$$

- Add in volume exclusion.