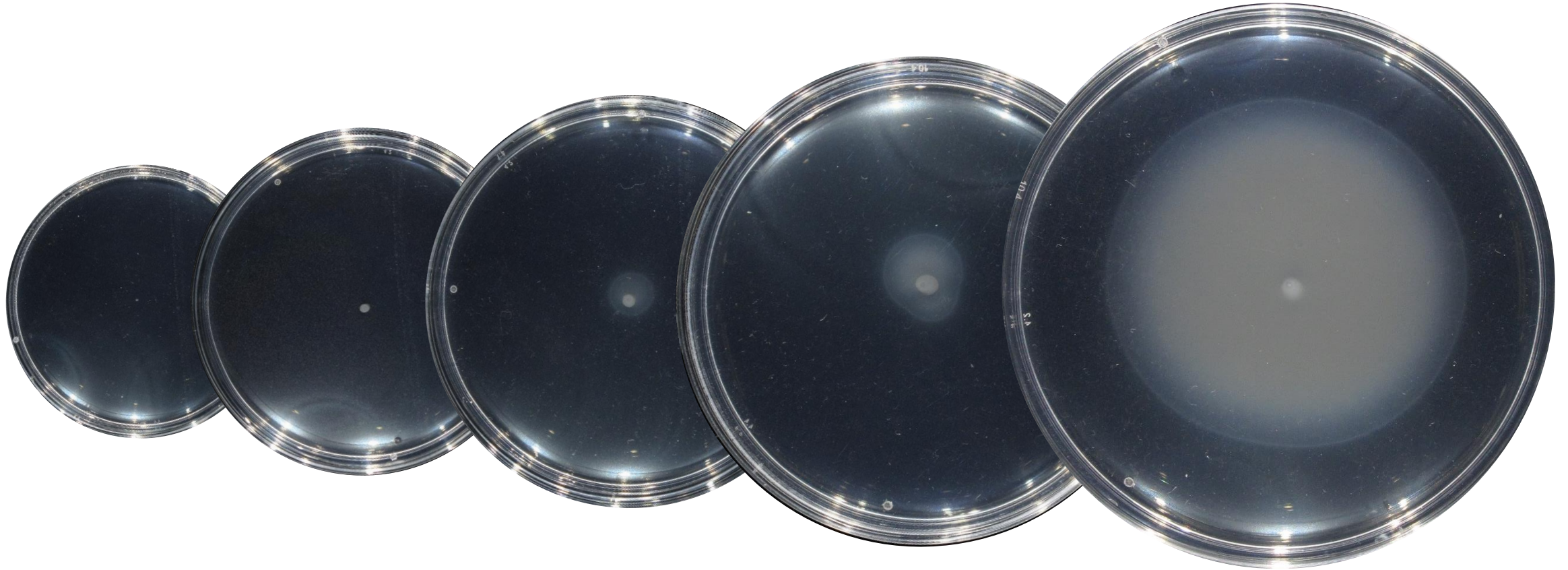


Experimental evolution: problems involving digital imaging and dynamic gene networks



Milner Centre for
EVOLUTION

Presented by:
Nick Priest
Milner Centre and B&B

Collaborators:
James Horton 1YPhD
Dr. Tiffany Taylor



UNIVERSITY OF
BATH

About me

My research:
How infection shapes evolution.

1. How hosts fight infection.
(Nutrient balance)

2. How pathogens evolve.

Emergence of migration
Regulatory Network Evolution





Cancer cell

Human cells mutate.

If they are not cleared, then regulatory network evolution leads to emergence of migration.

Big questions:

How long until migration?

Probability of regulatory network re-wiring?



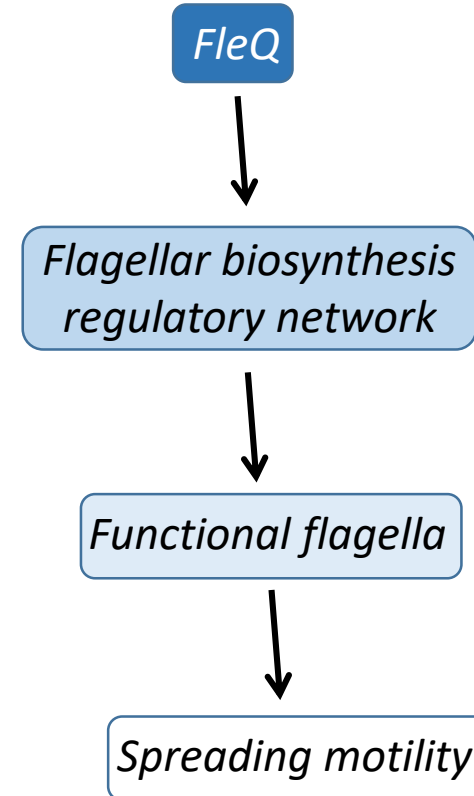
About the system



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Immotile strain AR2 (derived from SBW25):

- **FleQ** – Deleted from genome
- **Viscosin** – Interrupted by transposon-insertion



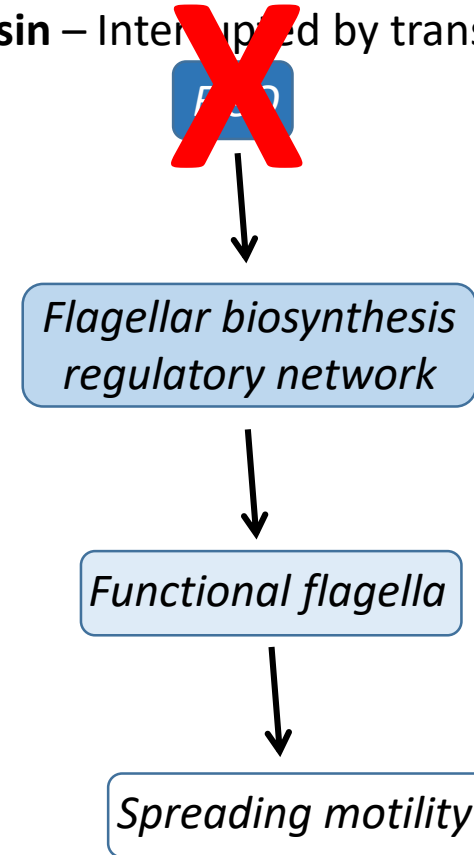
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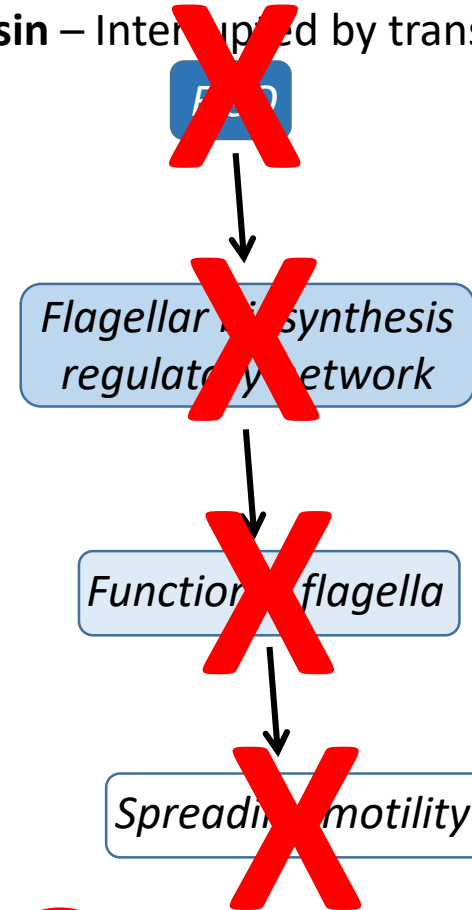
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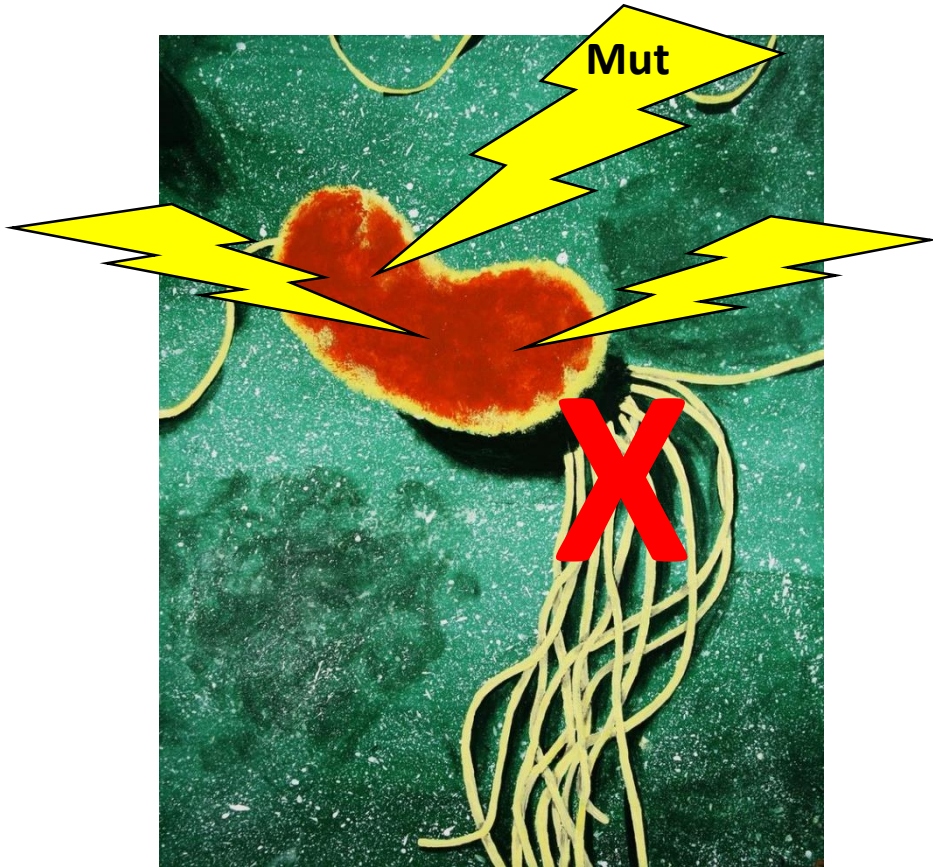
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It can't move

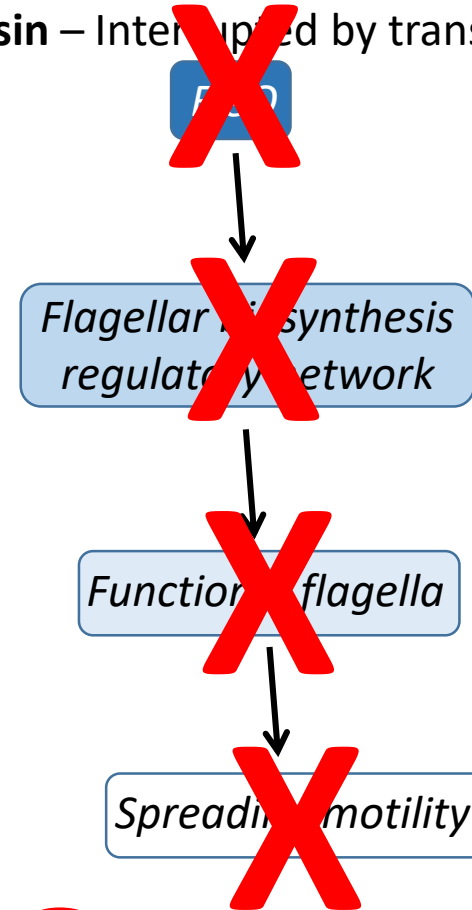
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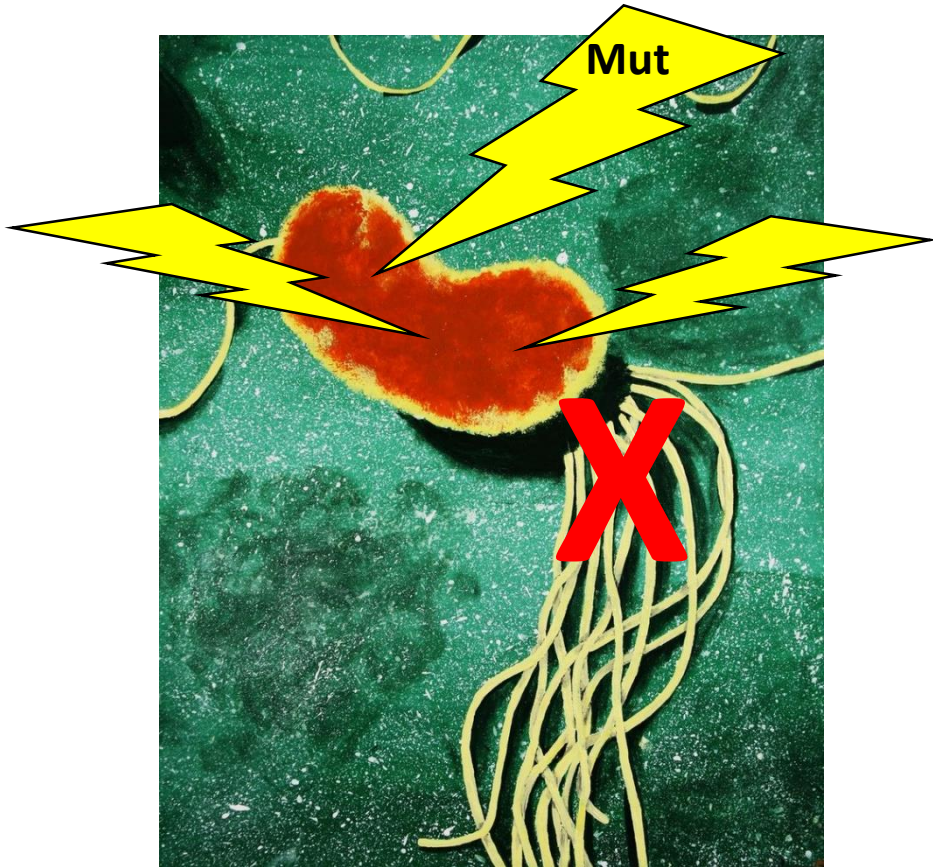
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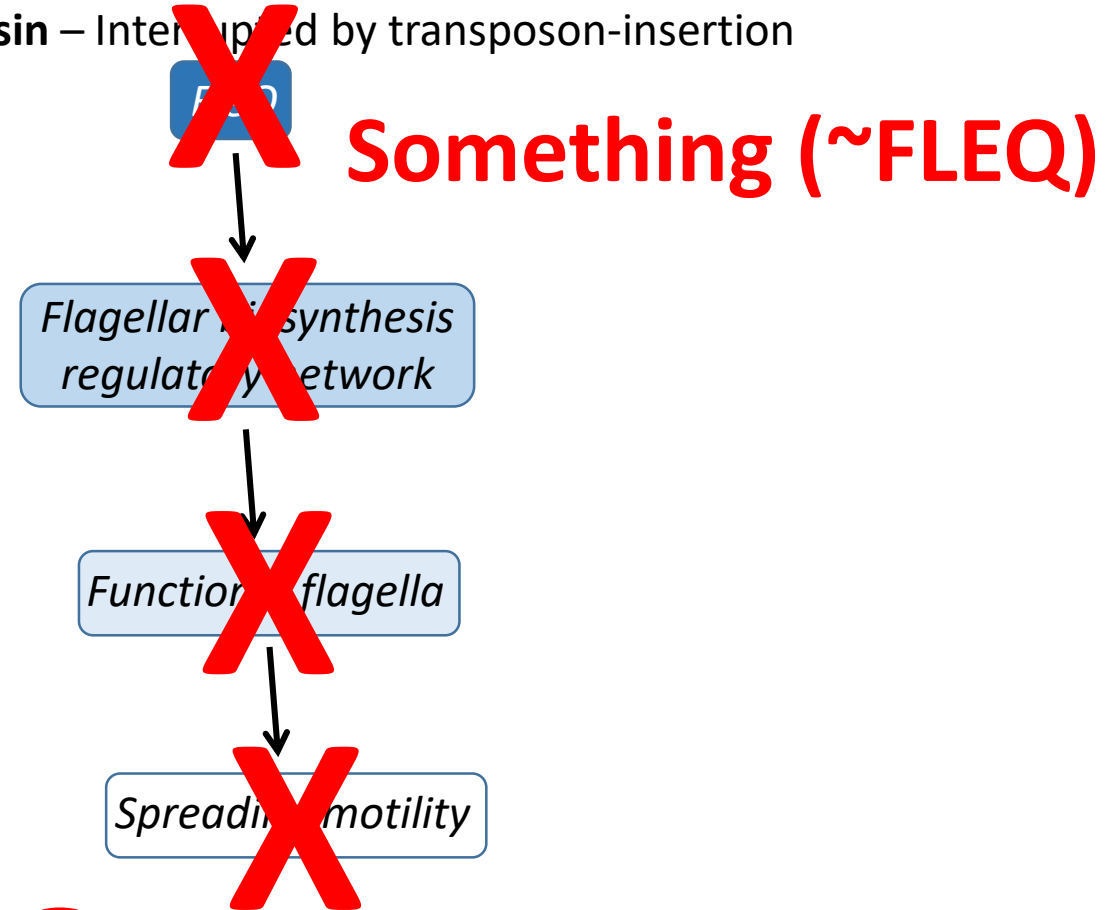
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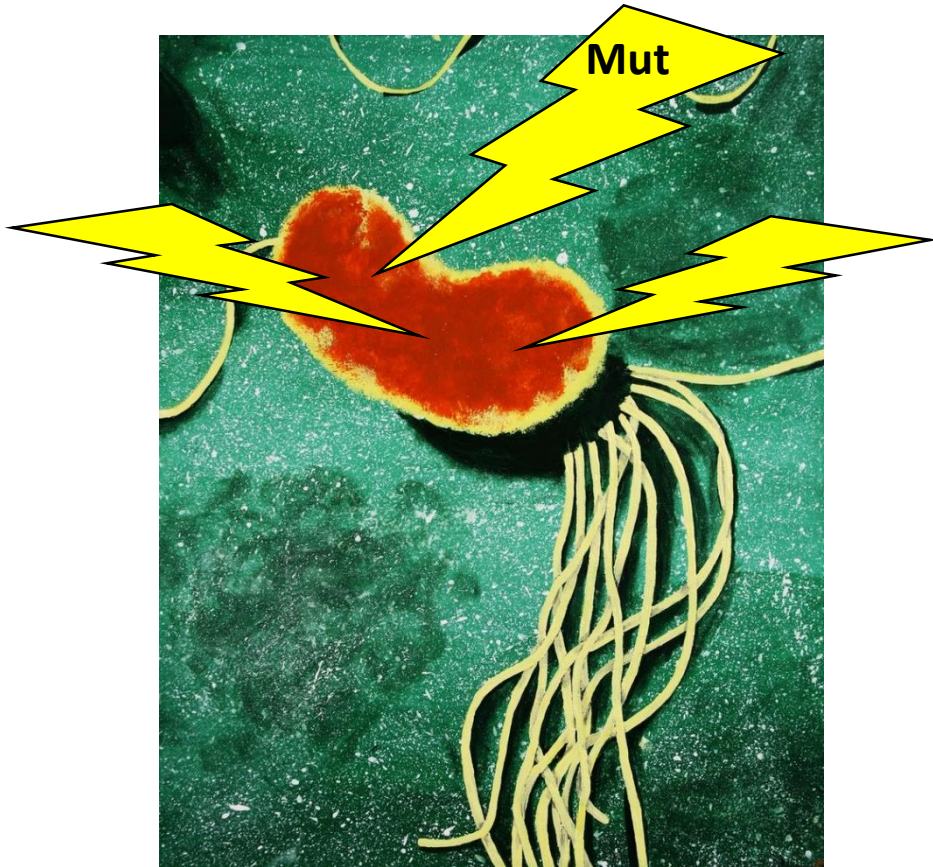
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Immotile strain AR2 (derived from SBW25):

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~~FleQ~~ **Something (~FLEQ)**

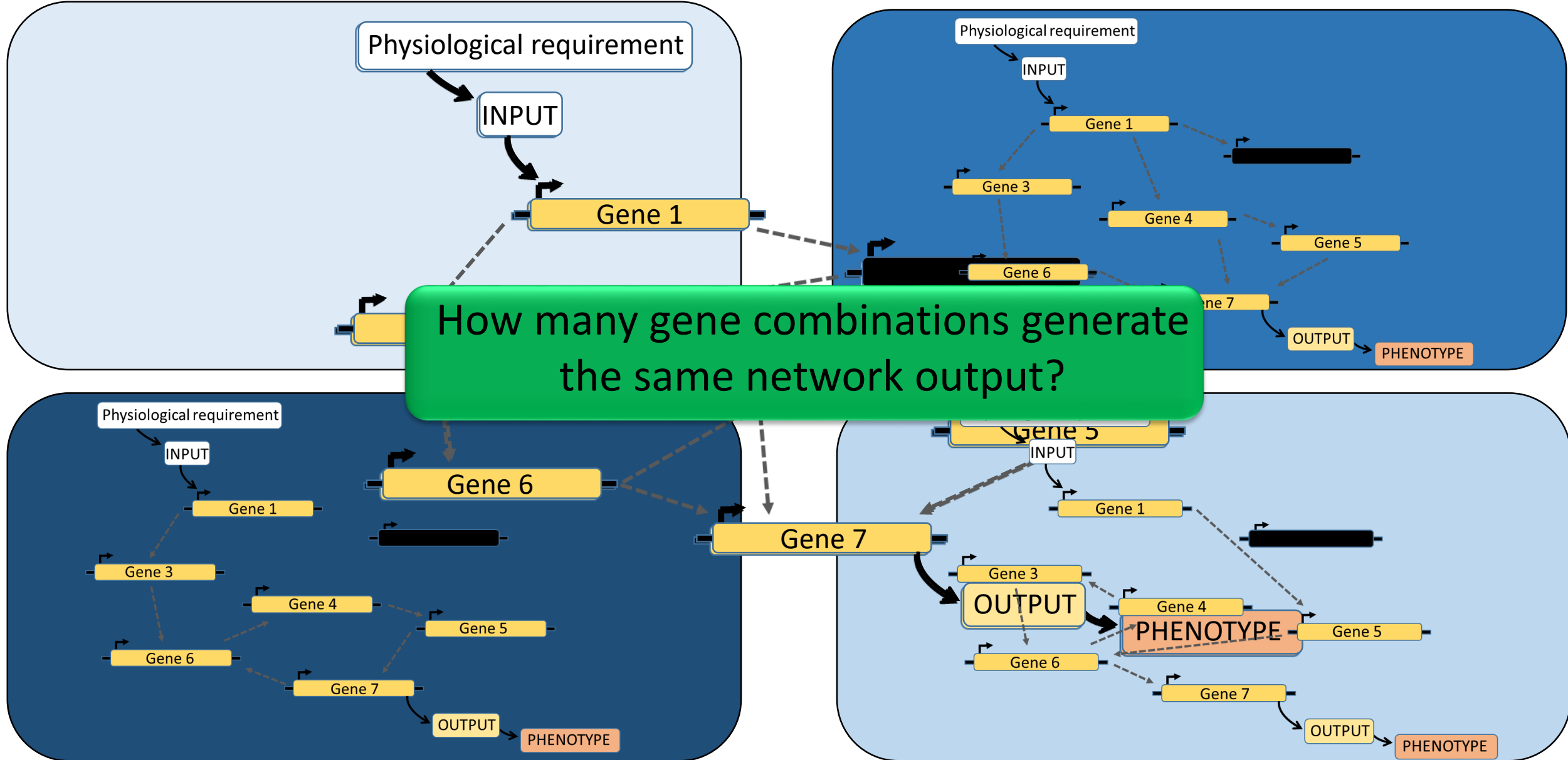
*Flagellar biosynthesis
regulatory network*

Functional flagella

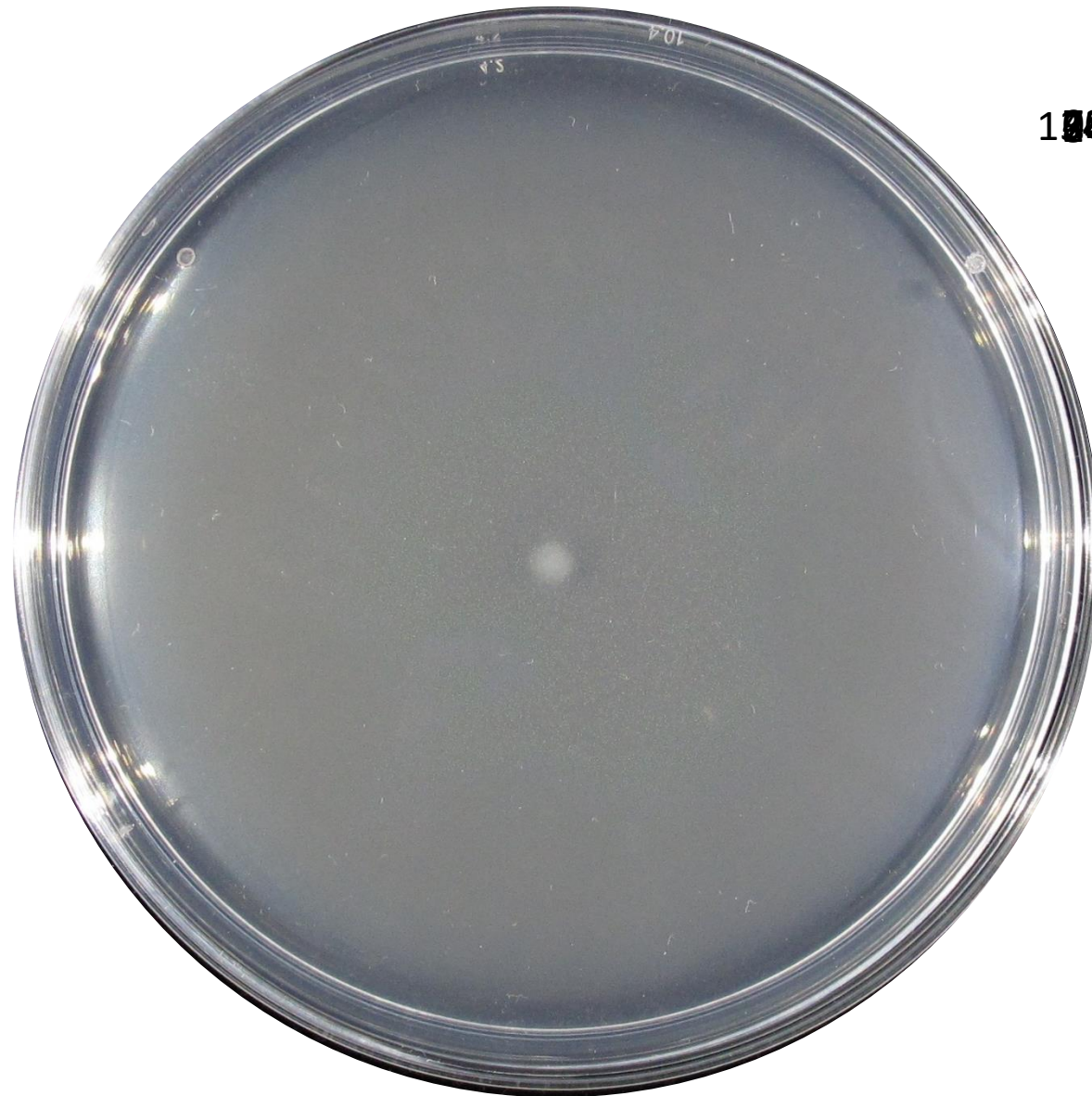
Spreading motility

It moves!

An Introduction to Gene Regulatory Networks



Flagellar resurrection following starvation-driven selection

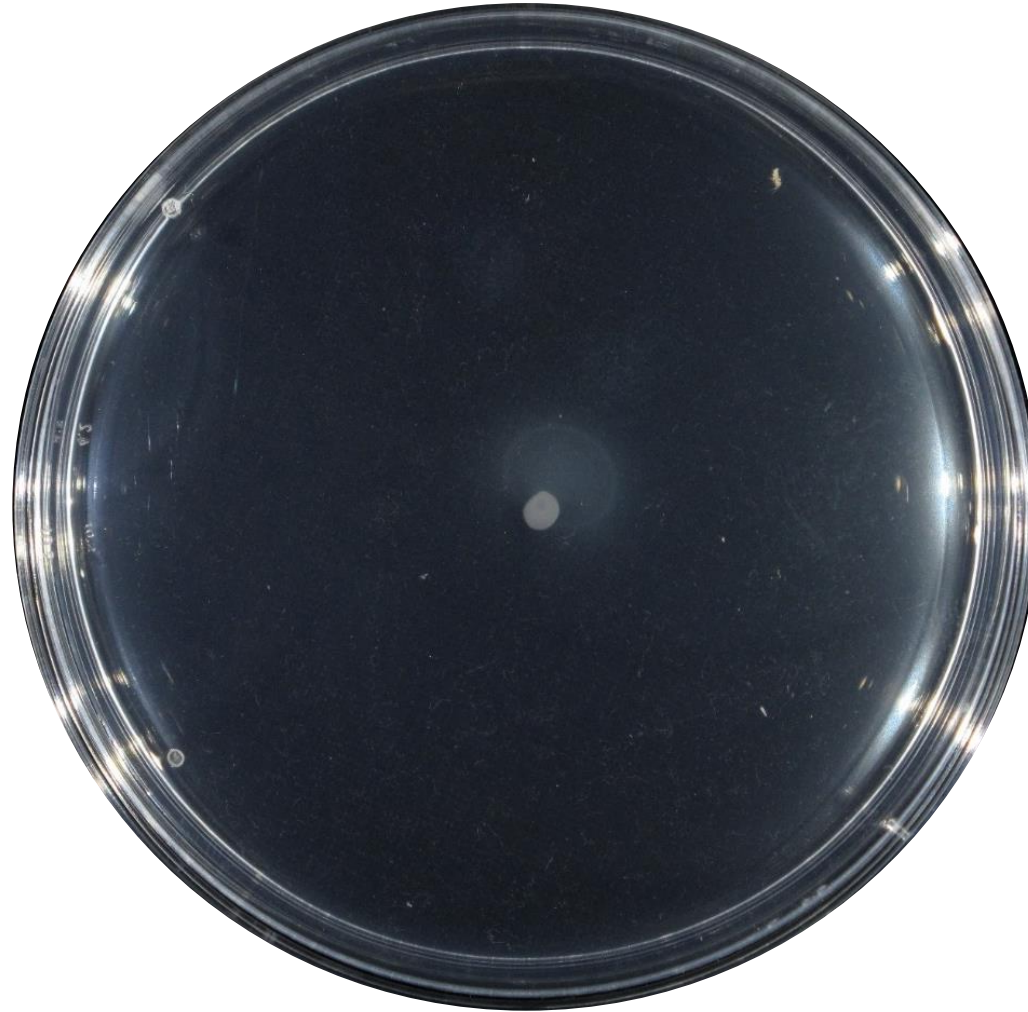


100 hours

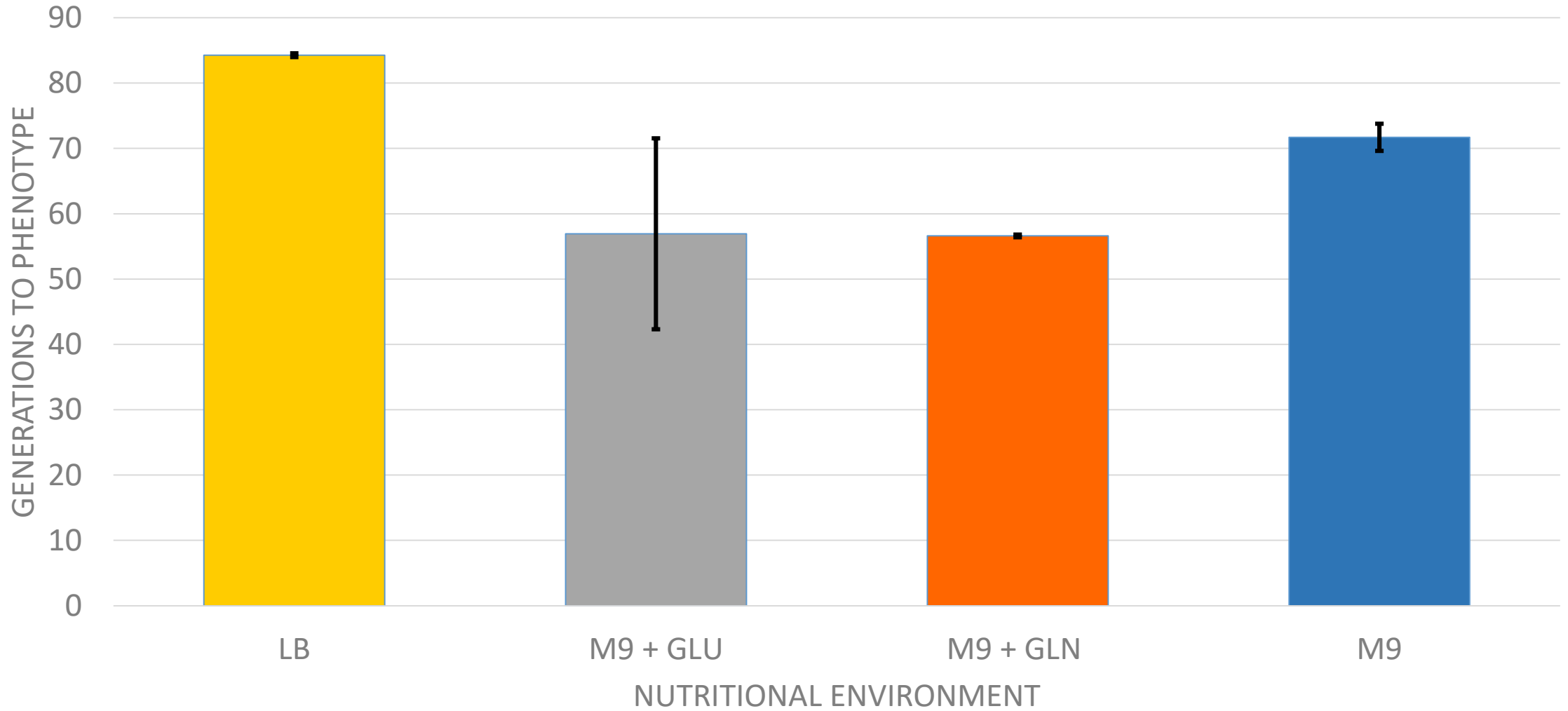
Question 1:

From digital images can we calculate when migration arises?

Extra: when second site, fast migration arises?



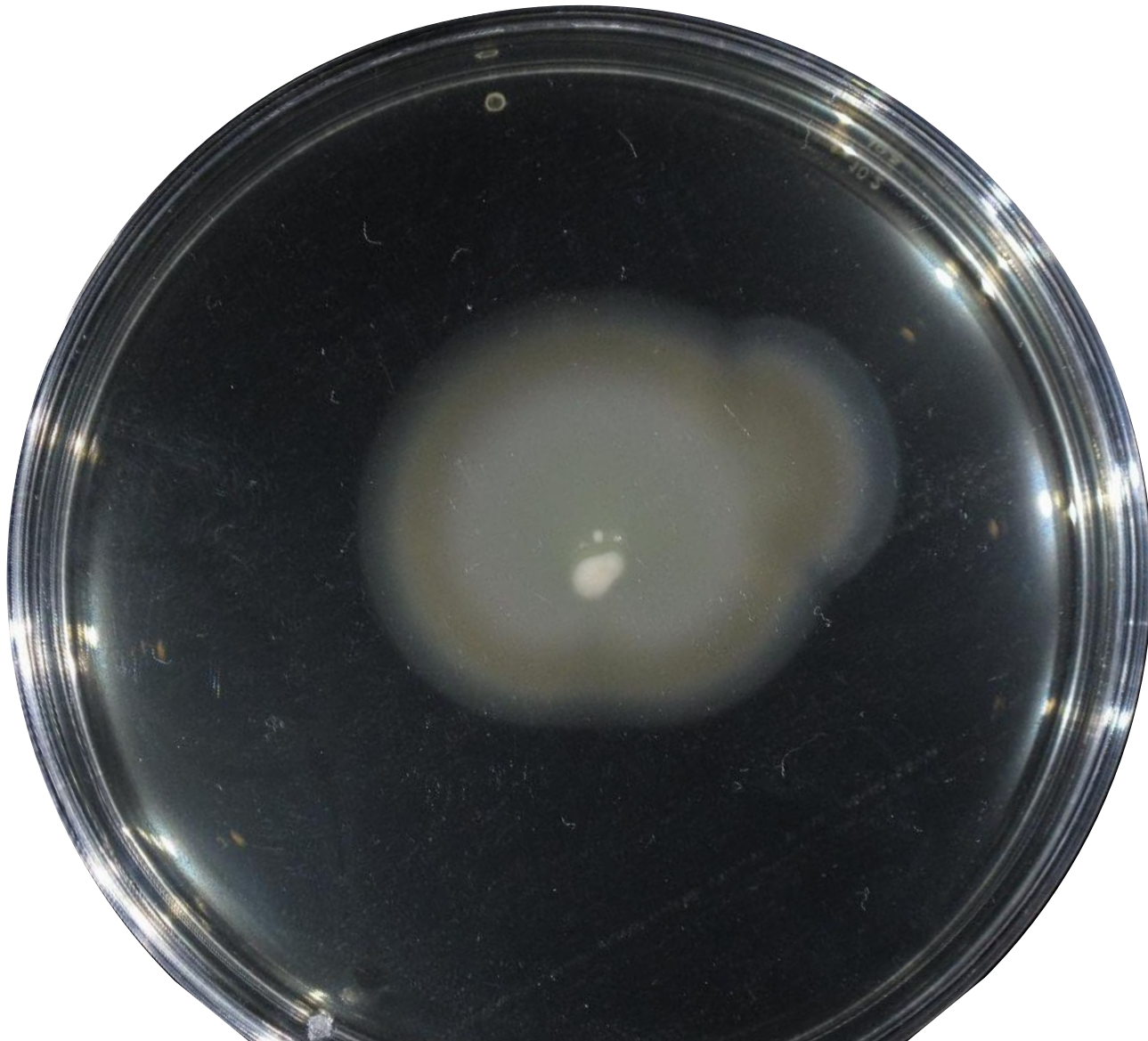
Current estimates



Question 1:

From digital images can we calculate when migration arises?

Extra: when second site, fast migration arises?



Fast-spread phenotype:

The two-step pathway:

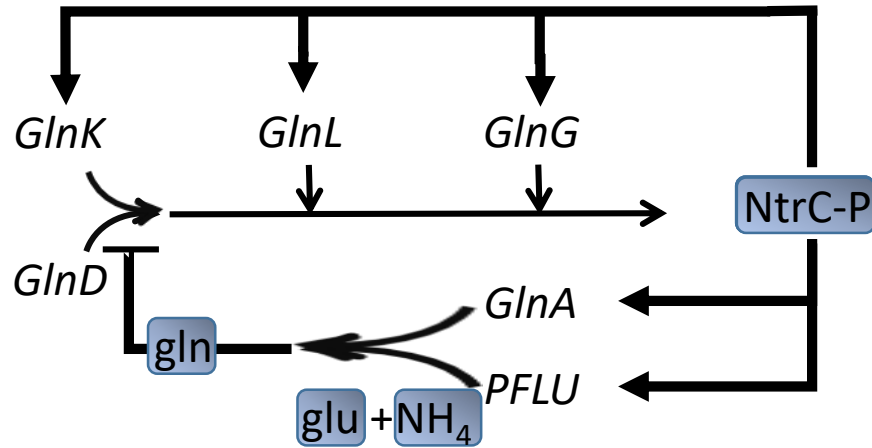
Question 2:

**How many ways to rewire a network?
Which mutations restore motility?**

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Nitrogen assimilation network (immotile strain)



KEY

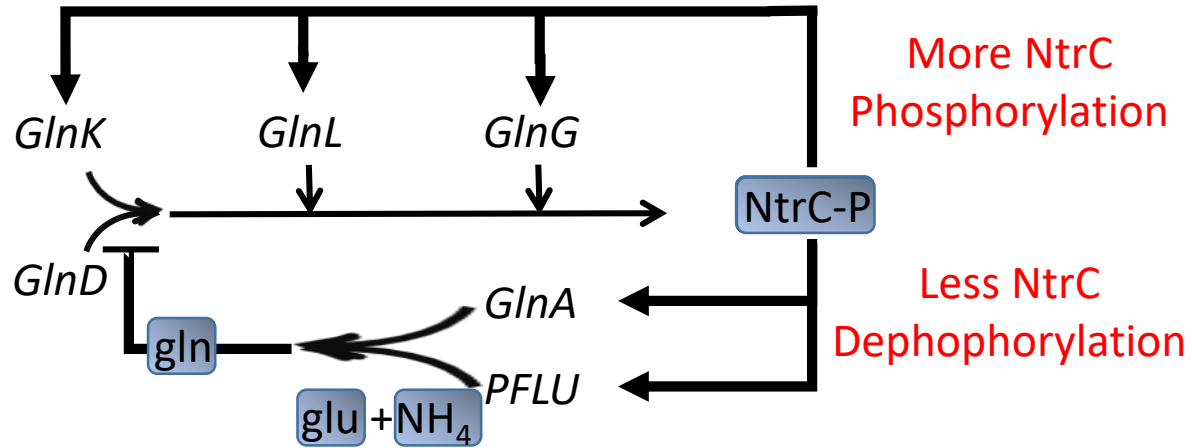
GlnG -- Genes

glu -- Molecules

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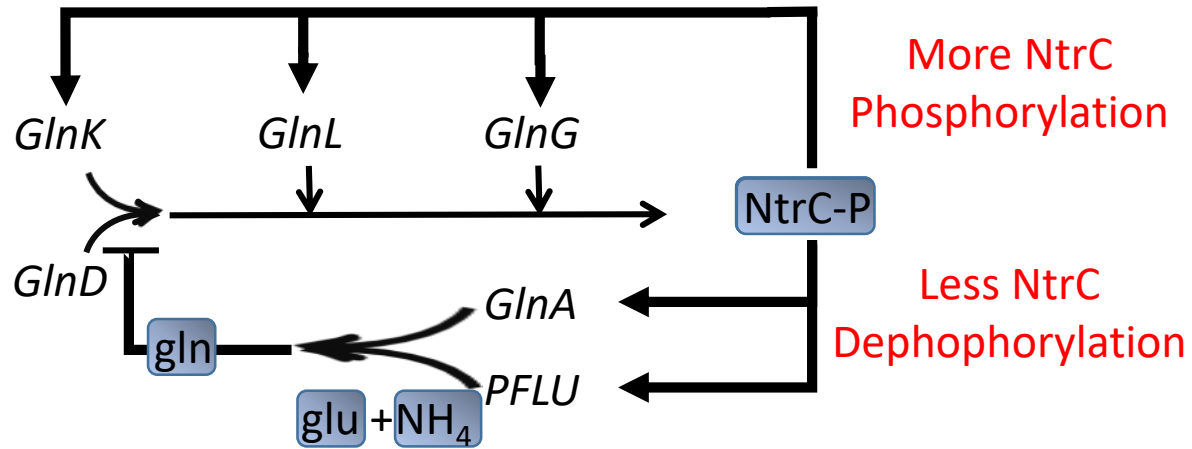
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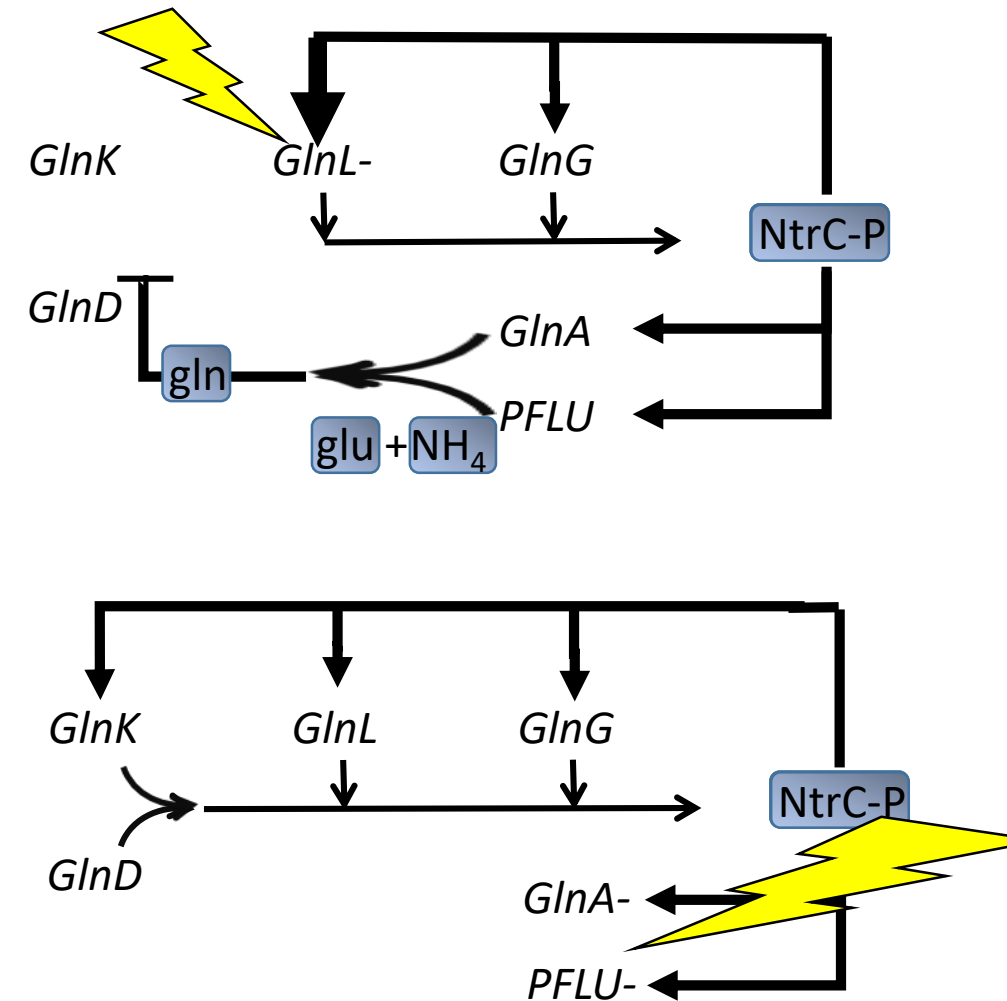


KEY

GlnG -- Genes

glu -- Molecules

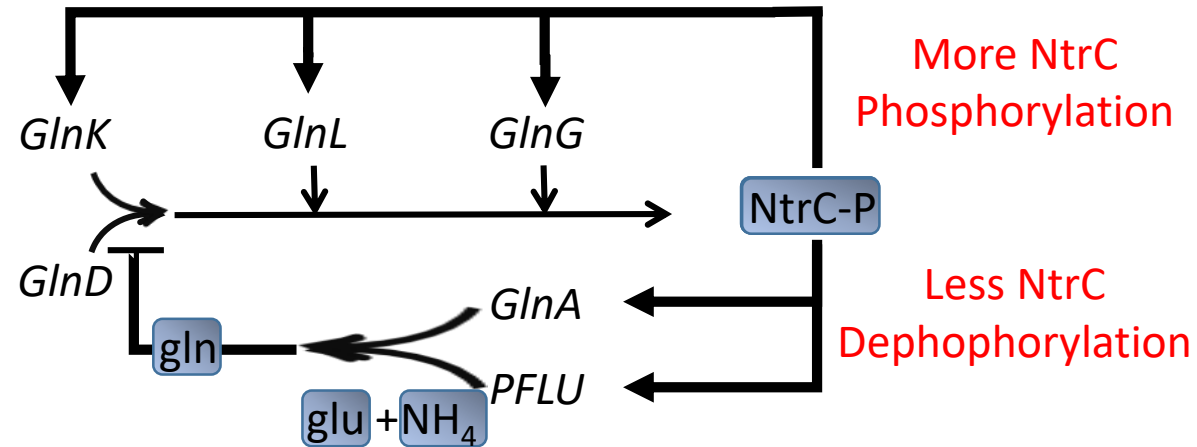
Motile strains



Question 2:

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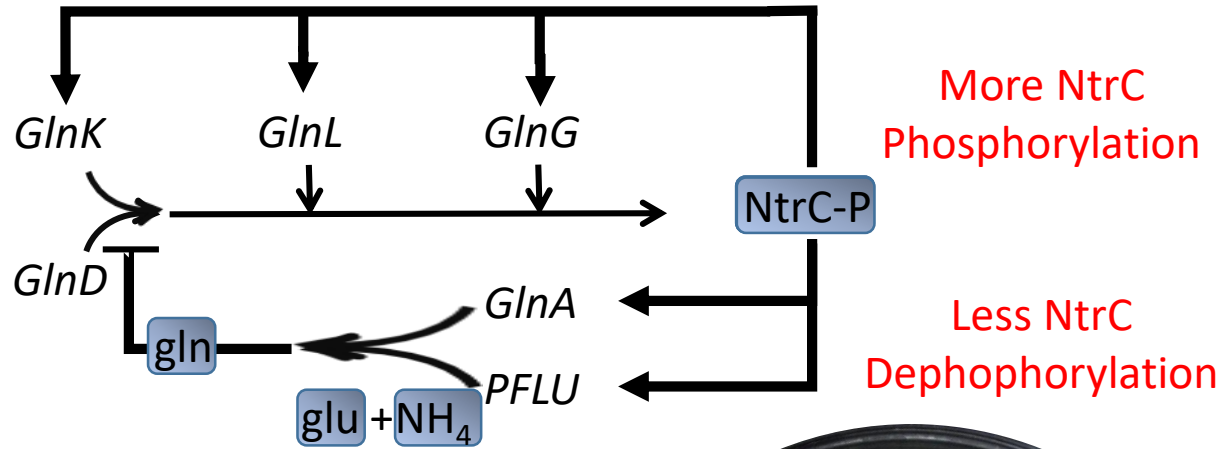


Extras

Question 2:

How many ways to rewire a network?
Which mutations restore motility?

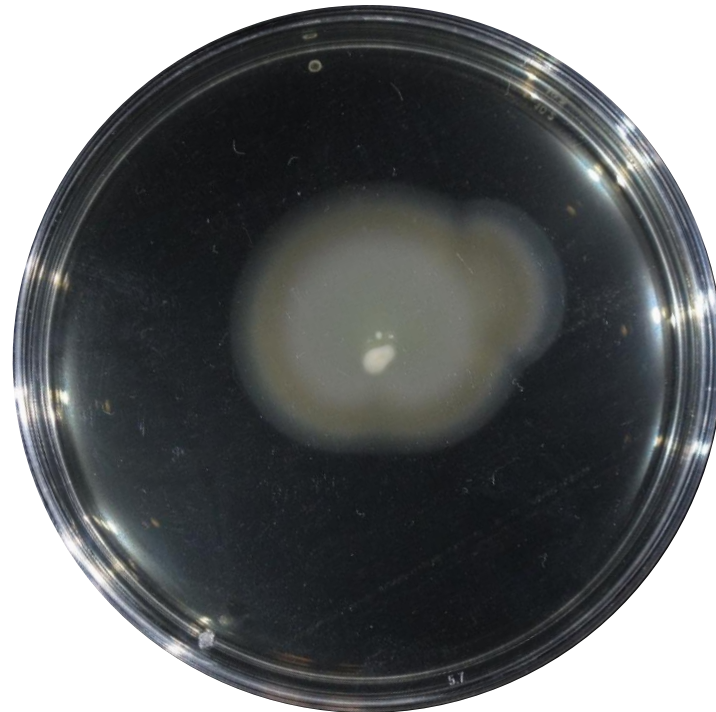
Nitrogen assimilation network (immotile strain)



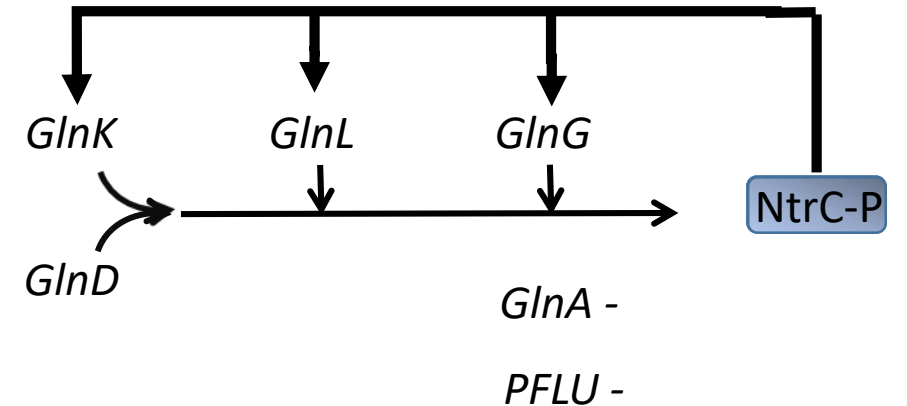
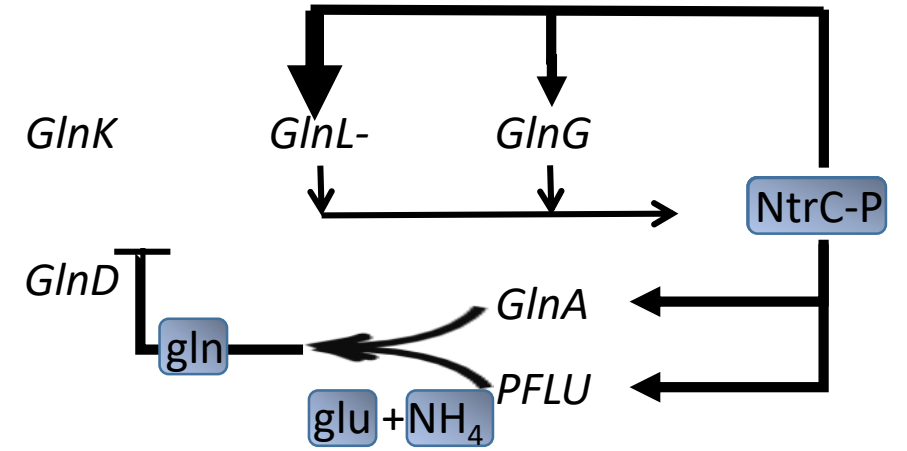
KEY

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glu -- Molecules

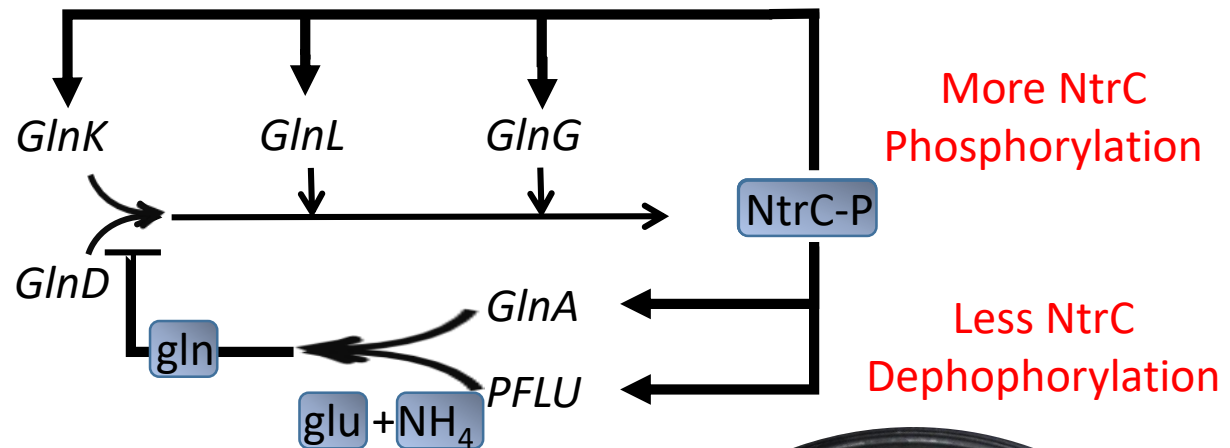


Motile strains



Question 2 Extras: Why *GlnG* for fast migration?

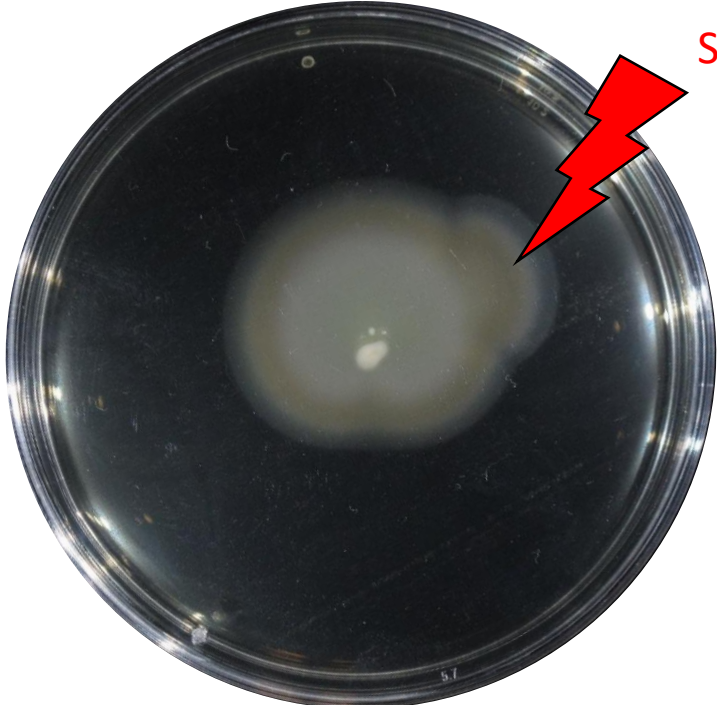
Nitrogen assimilation network (immotile strain)



KEY

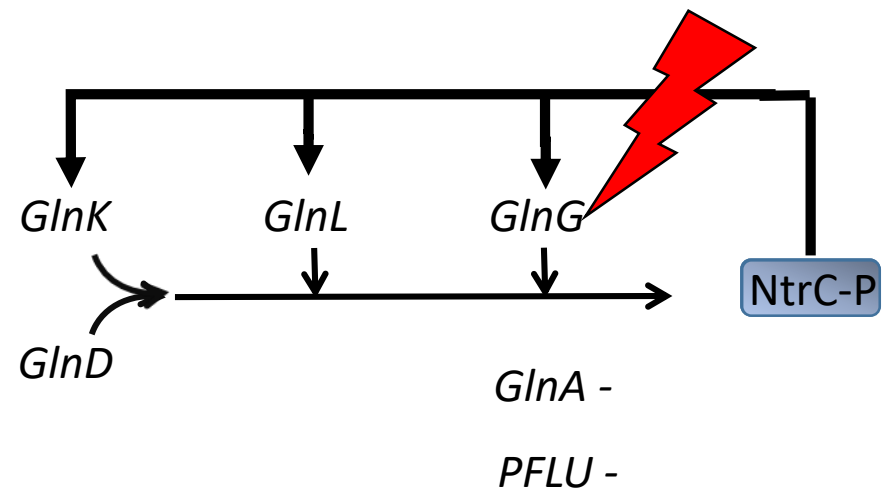
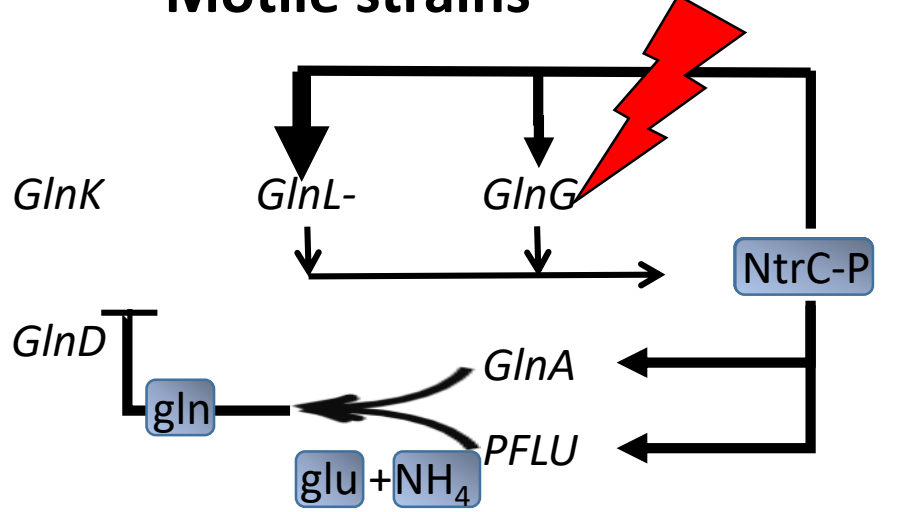
GlnG -- Genes

glu -- Molecules



Second Site mutation

Motile strains

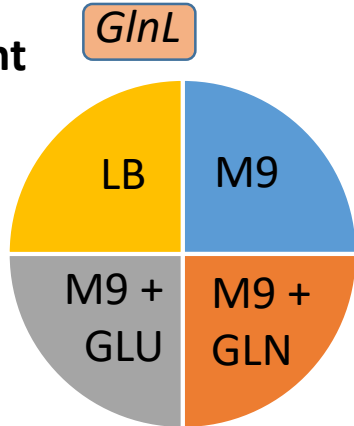


Question 2 Extras: Why does nutrition matter?

Immotile strains were grown in 4 environments:



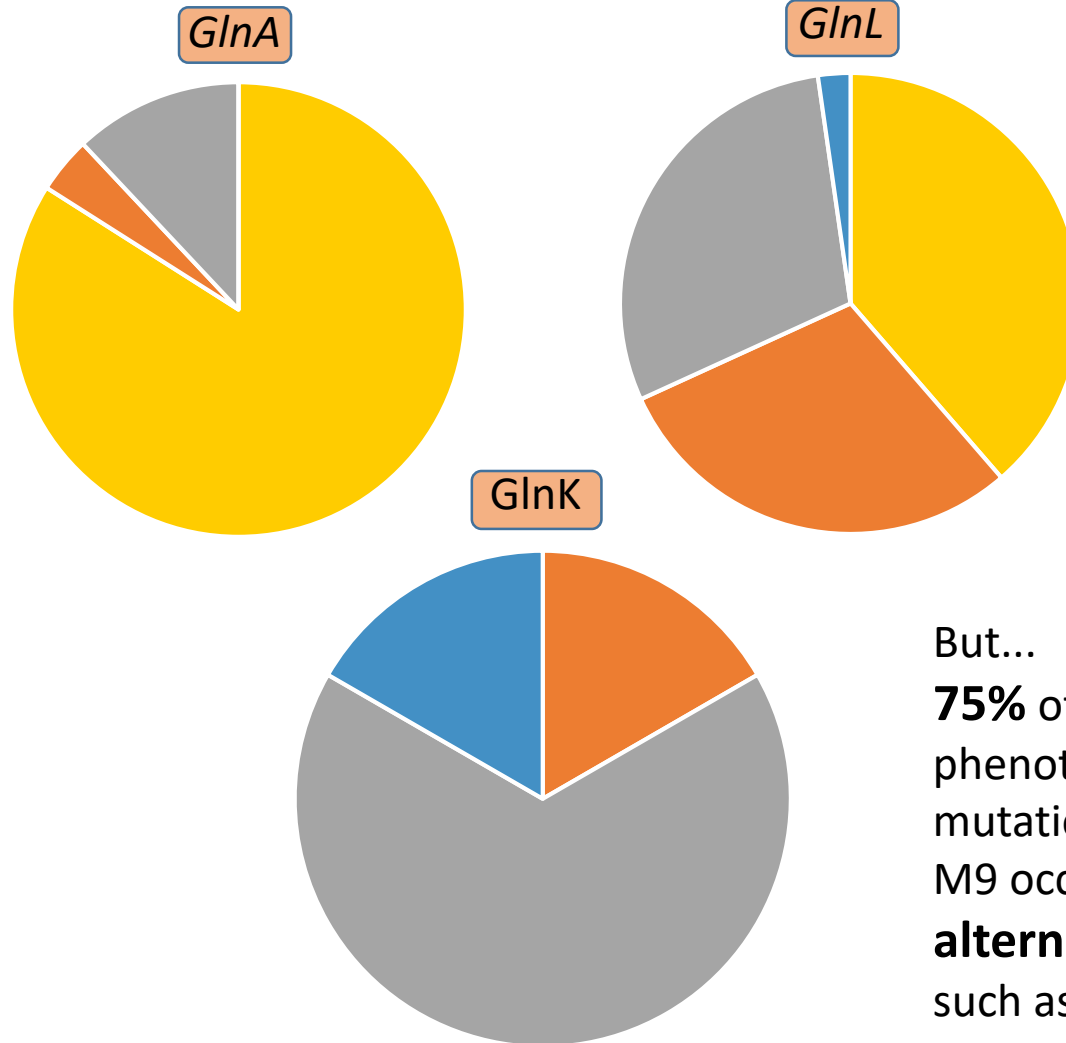
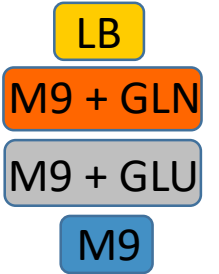
If the environment did not matter:



Fitness assays:

| | | |
|-----|------------|-------------------|
| LB | M9-evolved | Standard |
| GLU | | competitor strain |
| GLN | | |
| M9 | 50% | 50% |

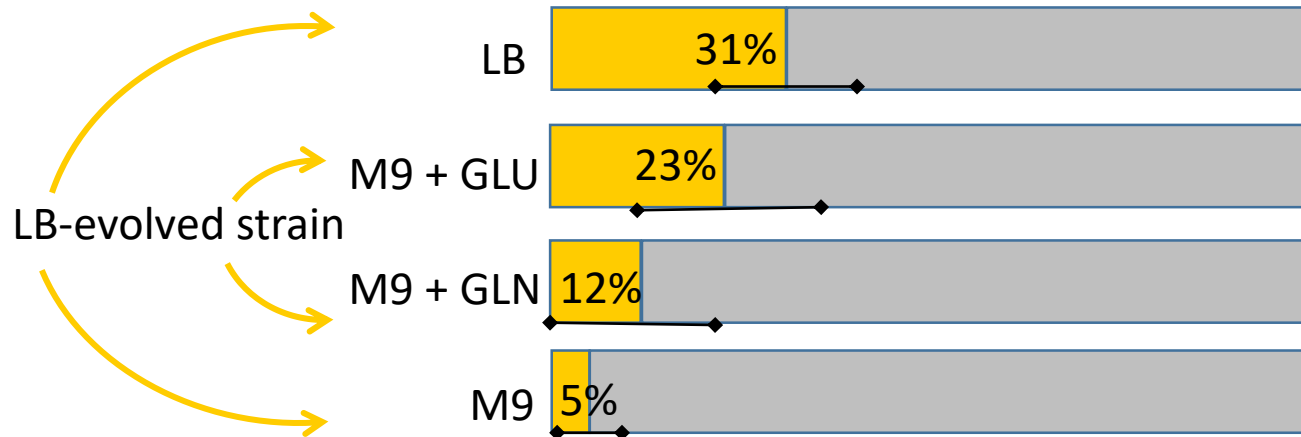
Strains evolved in:



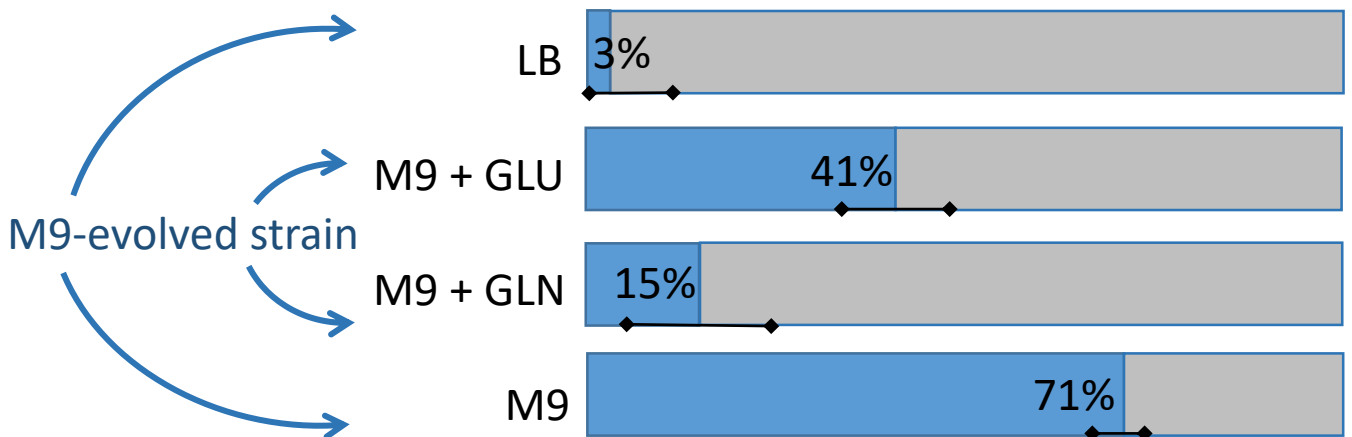
But... **75%** of all phenotype-saving mutations grown in M9 occurred in **alternative genes**, such as *pflu5952*

Question 2 Extras: Why does nutrition matter?

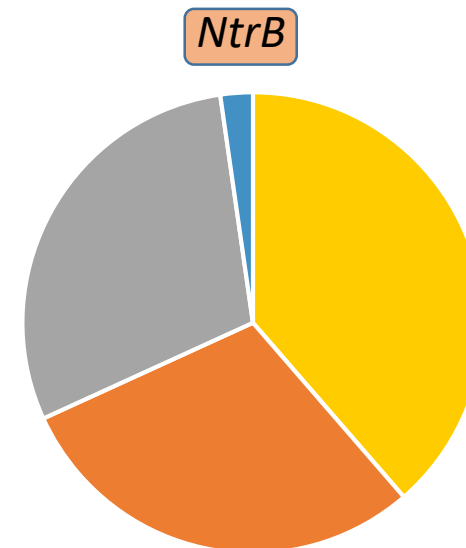
AR2SNP vs LB-evolved strain:



AR2SNP vs M9-evolved strain:



SNP competitor strain



But...
75% of all phenotype-saving mutations grown in M9 occurred in **alternative genes**, such as *pflu5952*

Human cells mutate.

If they are not cleared, then regulatory network evolution leads to emergence of migration.

Big questions:

How long until migration?

Probability of regulatory network re-wiring?



Acknowledgements and references

Collaborators:

James Horton
Tiffany Taylor

References:

Taylor, T., Mulley, G., Dills, A., Alsohim, A., McGuffin, L., Studholme, D., Silby, M., Brockhurst, M., Johnson, L. and Jackson, R. (2015). Evolutionary resurrection of flagellar motility via rewiring of the nitrogen regulation system. *Science*, 347(6225), pp.1014-1017.



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Restoring motility phenotype – FleQ is essential for flagellar motility

Motility and swarming are facilitated by two key factors:

~~FleQ~~ – the master regulator of *flg* genes, responsible for flagellar biosynthesis and swarming motility.

~~Viscosin~~ – a biosurfactant that facilitates sliding surface motility even in the absence of FleQ via a ‘spidery spreading’ phenotype.

For our study FleQ was deleted, and viscosin disrupted via transposon-insertion.

