

An Introduction to Flux Balance Analysis Using Pathway/Genome Databases

Ranjan Srivastava

SRI

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Research Focus

- Identification of potential drug targets for pathogens
- Development of inhibitory RNA therapeutics

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 - Genome-scale flux balance analysis
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 - Dynamic flux balance analysis
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Metabolic Chokepoints

- 274/377 chokepoints identified for malaria

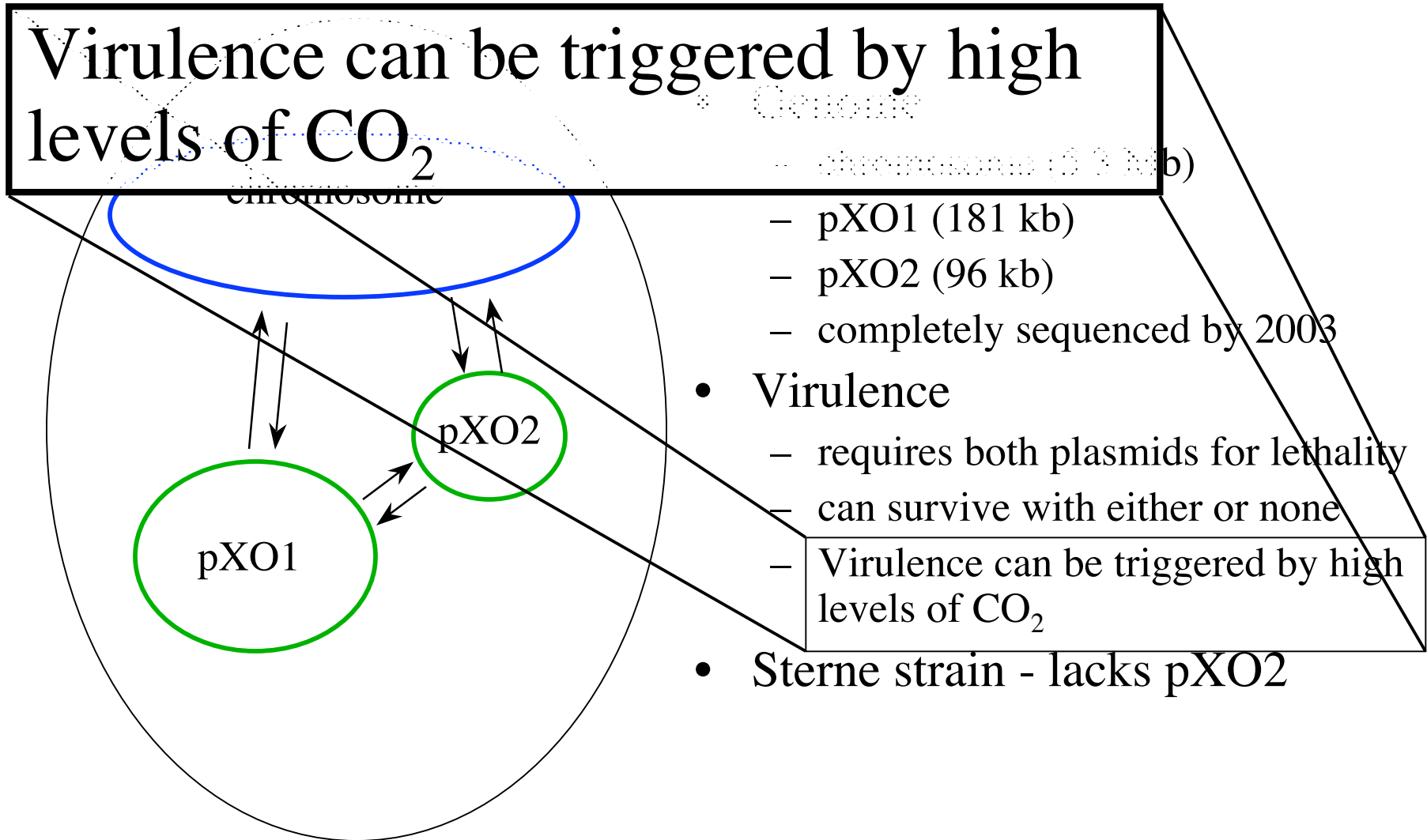
How many of those pathways
are active during virulence?

History of Anthrax

- Ancient Egypt -
Plague of Boils
(1500 BC)
- Known to ancient
Greeks & Romans
(Homer ~ 1200 BC,
Virgil ~ 60 BC)
- Mentioned in early
Hindu literature
(500 BC)



B. anthracis Molecular Biology



Genome-scale Flux Analysis

\bar{X} = metabolites

\bar{r} = reaction

μ = growth rate

$$\frac{d\bar{X}}{dt} = \bar{r} - \mu\bar{X}$$

$$\bar{0} = \bar{r}$$

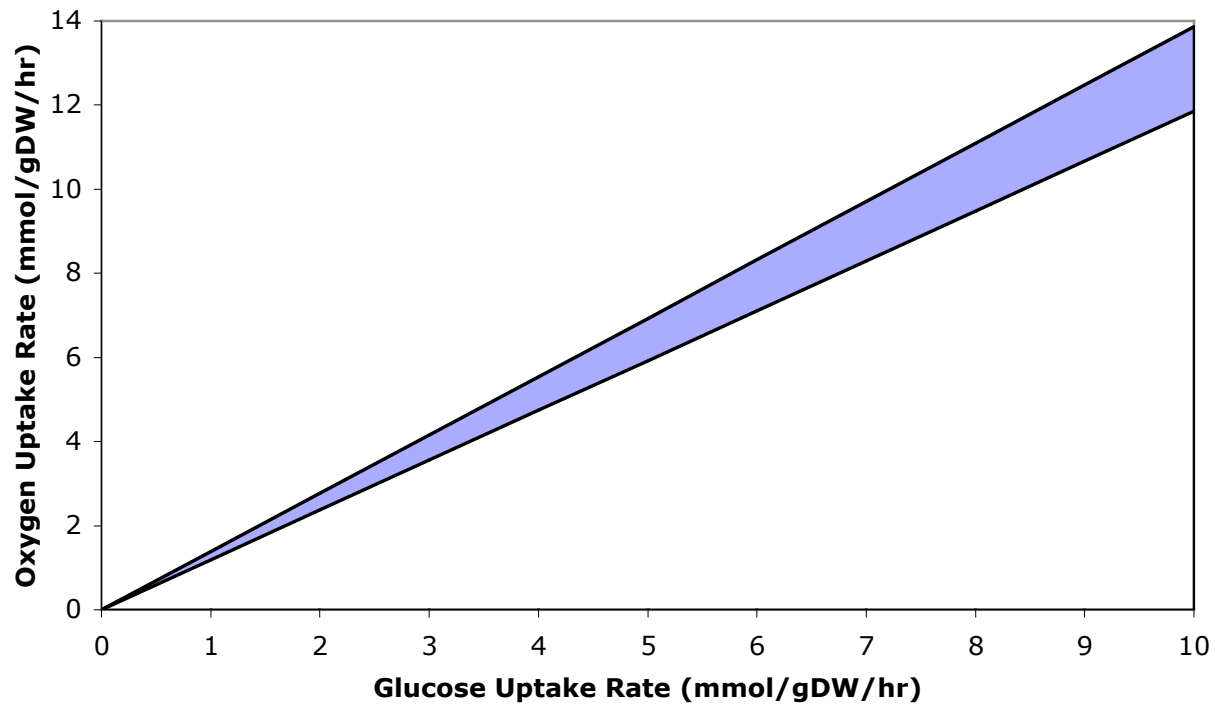
\bar{S} = stoichiometric matrix

\bar{v} = metabolic flux vector

$$\bar{r} = \bar{S}^T \bar{v}$$

$$\bar{0} = \bar{S}^T \bar{v}$$

Feasible Growth Regime for *B. anthracis*



Defined complex media

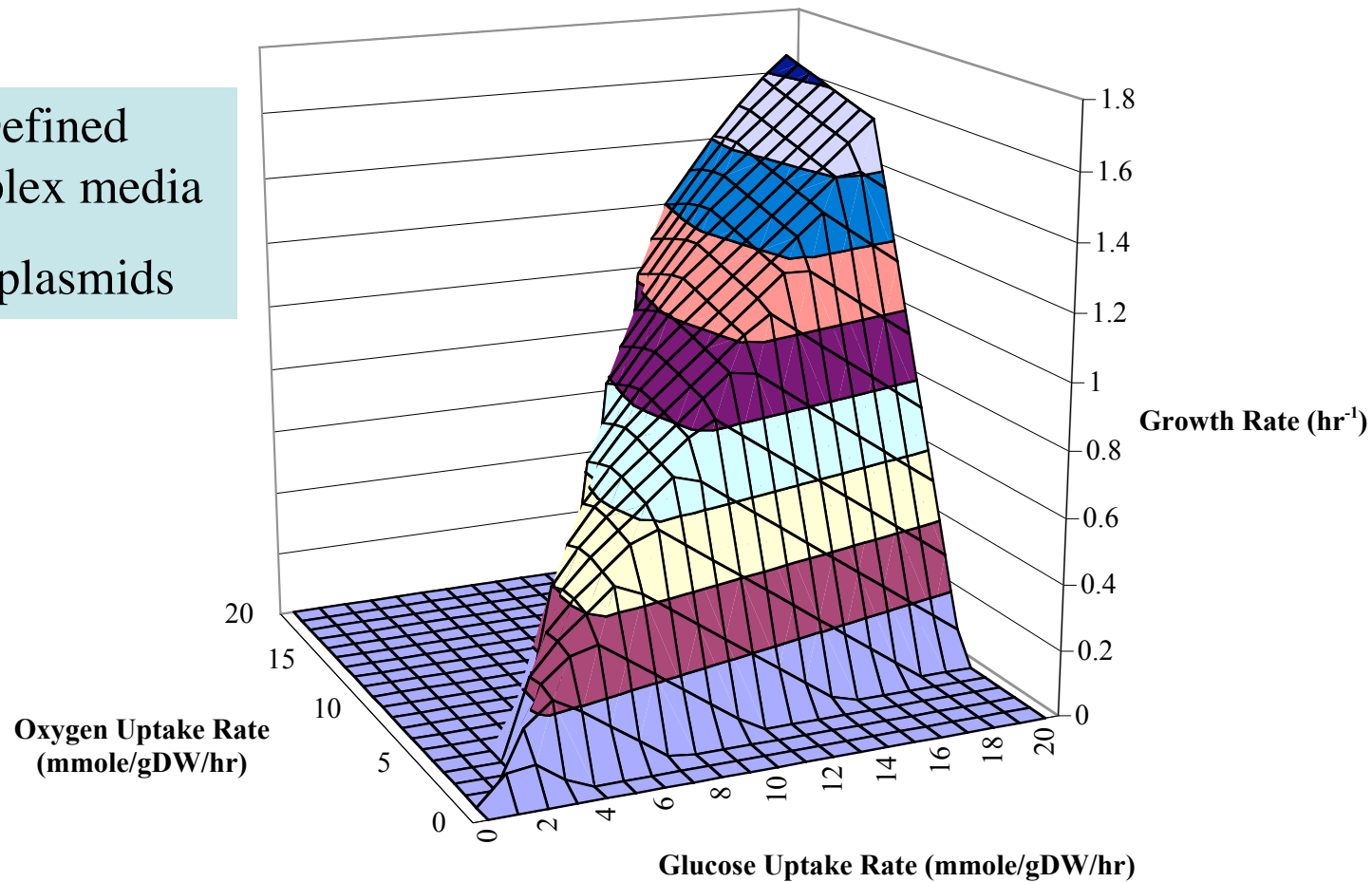
No plasmids

Potential objective functions

- Maximization of growth rate
- Minimization of redox potential
- Minimization of ATP production
- Minimization of nutrient uptake
- Minimization of acetate overflow

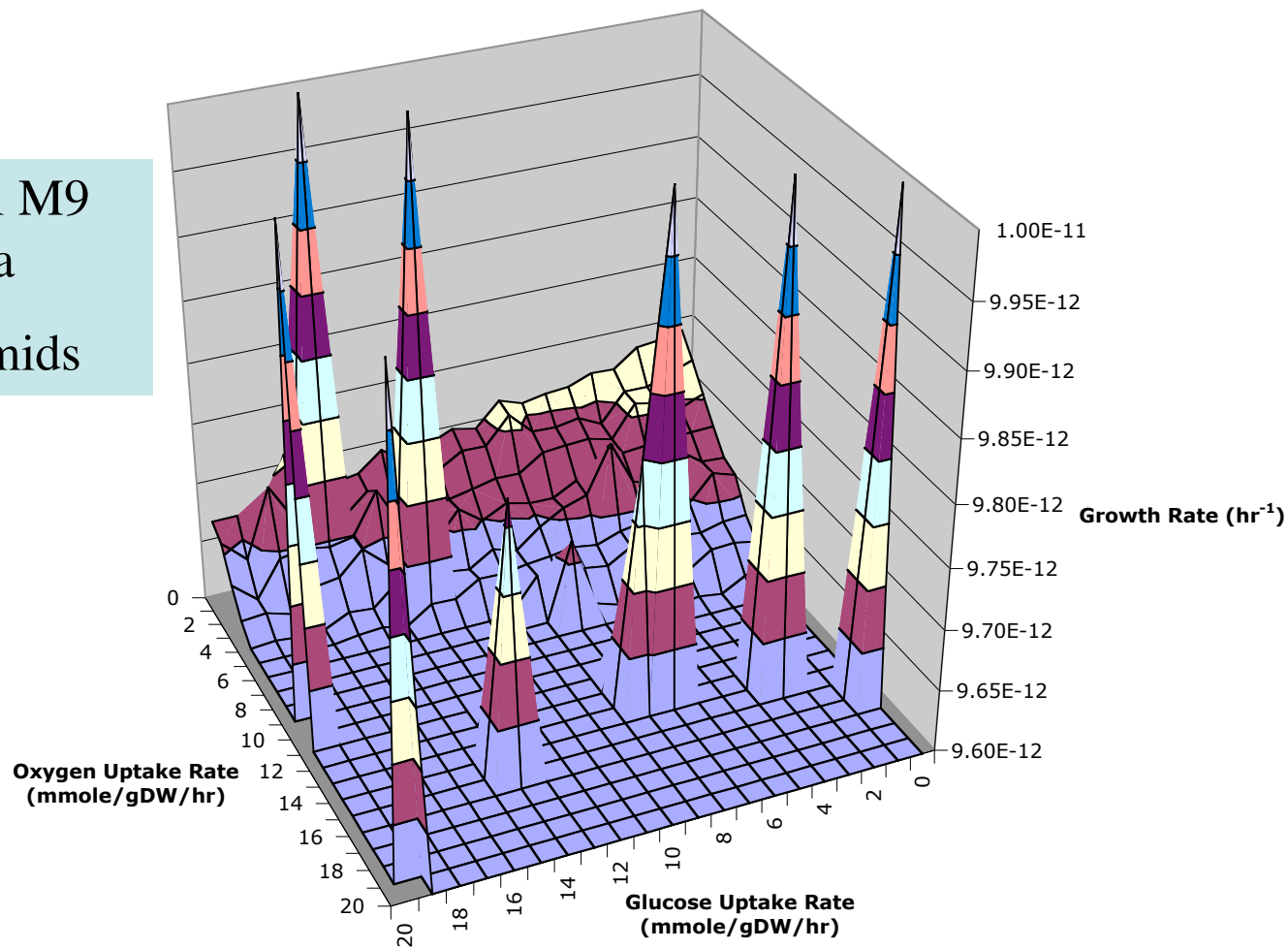
Predicted Growth Rate for *B. anthracis*

Defined
complex media
No plasmids



Predictions for Growth on Minimal M9 Media

Minimal M9
media
No plasmids



Why automated FBA?

- Generate FBA on the fly
- Keep up to date with latest PGDB
- Comparative analysis
- Generate a reference FBA (*E. coli*)
- Ideally, shouldn't need to be an “expert” to carry out FBA

Issues

1. Reactions listed twice under different names or EC#s
2. Reactions with non-specific metabolites, such as “lipoprotein” or “enzyme”
3. Improper stoichiometry
4. Many reactions are not hydrogen balanced
5. Reversibility
6. Incomplete EC#s
7. Need more transport reactions

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