**Flux Balance Analysis**

\[
\begin{align*}
\text{max } \quad & v_{\text{obj}} \\
\text{subject to } \quad & S v = 0 \\
\quad & l \leq v \leq u
\end{align*}
\]

Images courtesy of T. Shlomi
Genome-scale models can predict steady-state metabolic phenotypes from limited kinetic data.

reaction fluxes optimize the metabolic objective
Genome-scale models can predict steady-state metabolic phenotypes from limited kinetic data.

reaction fluxes optimize the metabolic objective

Solutions must obey stoichiometric (mass balance), thermodynamic, and physiological constraints.
Genome-scale models can predict steady-state metabolic phenotypes from limited kinetic data.

Genes are represented as "on" or "off".
Genome-scale models can predict steady-state metabolic phenotypes from limited kinetic data.

Genes are represented as "on" or "off"
*Pseudomonas aeruginosa*: an emerging health threat.

Gram-negative **opportunistic** human pathogen

Significant healthcare burden

- Burn patients, immunocompromised individuals
- Catheter and medical device implants
- Endemic in cystic fibrosis patients
- Notorious for nosocomial infections
  (10% of all hospital-acquired infections)

High metabolic versatility (aerobic & anaerobic)

Antibiotic resistance
Genome-Scale Metabolic Network Analysis of the Opportunistic Pathogen *Pseudomonas aeruginosa* PAO1

Matthew A. Oberhardt,‡‡ Jacek Puchalka,‡§ Kimberly E. Fryer,‡
Vitor A. P. Martins dos Santos‡§ and Jason A. Papin§*

1086 genes
1136 reactions
1021 metabolites
52 subsystems
Predicting novel antibiotics using a metabolic network model.

DrugBank / KEGG drug/target interaction databases + PAO1 genome = iMO1086 PAO1 model

PAO1 drug/gene mapping

gene essentiality

Antibiotic Predictions
Predicting novel antibiotics using a metabolic network model.

DrugBank / KEGG
drug/target interaction databases

10,000 drugs

PAO1 genome
6,000 genes

iMO1086 PAO1 model
1,086 genes

PAO1 drug/gene mapping

gene essentiality

24 prioritized drugs
13 experimentally validated hits

Antibiotic Predictions
Alendronic acid inhibits *P. aeruginosa* growth *in vitro* across a wide range of clinical isolates.

**Predicted target:** farnesyl pyrophosphate synthetase (PA4569)