

## 2. Introduction to Metabolic Modelling

David Fell  
OXFORD  
**BROOKES**  
UNIVERSITY

email: [dfell@brookes.ac.uk](mailto:dfell@brookes.ac.uk)

<https://mudshark.brookes.ac.uk>

November 29, 2024

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

Model Formulation

A little mathematics

Summary

# Preamble

# Complicated or Complex?

## Preamble

- **Complicated or Complex?**

- Modelling and Simulation

- Simulated Life

- Virtual Biochemistry

- Why Model

Metabolism?

- Industrial

Biotechnology and Synthetic Biology

- Design Issues in Synthetic Metabolism

- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- When scientists or engineers study a discrete entity, they can often find a mathematical or verbal description of its behaviour that can be used to predict its response in different circumstances.

# Complicated or Complex?

## Preamble

- **Complicated or Complex?**

- Modelling and Simulation

- Simulated Life

- Virtual Biochemistry

- Why Model Metabolism?

- Industrial

- Biotechnology and Synthetic Biology

- Design Issues in Synthetic Metabolism

- Aims of Modelling

- Model Formulation

## A little mathematics

## Summary

- When scientists or engineers study a discrete entity, they can often find a mathematical or verbal description of its behaviour that can be used to predict its response in different circumstances.
- However, if studying a system composed of interacting and possibly differing parts, it soon becomes increasingly difficult to find a simple, reliable description as the number of interactions rises, i.e. becomes more complicated.

# Complicated or Complex?

## Preamble

### ● **Complicated or Complex?**

- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- When scientists or engineers study a discrete entity, they can often find a mathematical or verbal description of its behaviour that can be used to predict its response in different circumstances.
- However, if studying a system composed of interacting and possibly differing parts, it soon becomes increasingly difficult to find a simple, reliable description as the number of interactions rises, i.e. becomes more complicated.
- This is even more so if the system is also complex, that is, it has properties that are not inherent in the components nor a simple aggregate of their properties.

# Complicated or Complex?

## Preamble

### ● **Complicated or Complex?**

- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- When scientists or engineers study a discrete entity, they can often find a mathematical or verbal description of its behaviour that can be used to predict its response in different circumstances.
- However, if studying a system composed of interacting and possibly differing parts, it soon becomes increasingly difficult to find a simple, reliable description as the number of interactions rises, i.e. becomes more complicated.
- This is even more so if the system is also complex, that is, it has properties that are not inherent in the components nor a simple aggregate of their properties.
- At this point we often turn to modelling and simulation.

# Modelling and Simulation

## Preamble

- Complicated or Complex?

- **Modelling and Simulation**

- Simulated Life

- Virtual Biochemistry

- Why Model

Metabolism?

- Industrial

Biotechnology and Synthetic Biology

- Design Issues in Synthetic Metabolism

- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Modelling is the process of making a tractable representation of a system that can be reasoned over or is computable.

# Modelling and Simulation

## Preamble

- Complicated or Complex?

- **Modelling and Simulation**

- Simulated Life

- Virtual Biochemistry

- Why Model

- Metabolism?

- Industrial

- Biotechnology and Synthetic Biology

- Design Issues in Synthetic Metabolism

- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Modelling is the process of making a tractable representation of a system that can be reasoned over or is computable.
- Simplification is intrinsic to modelling; the aim is to reduce the complicatedness of the representation without also losing any of the complexity of the system behaviour.
- i.e. Simplify enough, but not too much.



# Modelling and Simulation

## Preamble

- Complicated or Complex?

- **Modelling and Simulation**

- Simulated Life

- Virtual Biochemistry

- Why Model

- Metabolism?

- Industrial

- Biotechnology and Synthetic Biology

- Design Issues in Synthetic Metabolism

- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Modelling is the process of making a tractable representation of a system that can be reasoned over or is computable.
- Simplification is intrinsic to modelling; the aim is to reduce the complicatedness of the representation without also losing any of the complexity of the system behaviour.
- i.e. Simplify enough, but not too much.
- Simulation is an implementation of the model to produce an imitation of the system's behaviour.

# Simulated Life

## Preamble

- Complicated or Complex?
- Modelling and Simulation

## ● Simulated Life

- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary



# Virtual Biochemistry

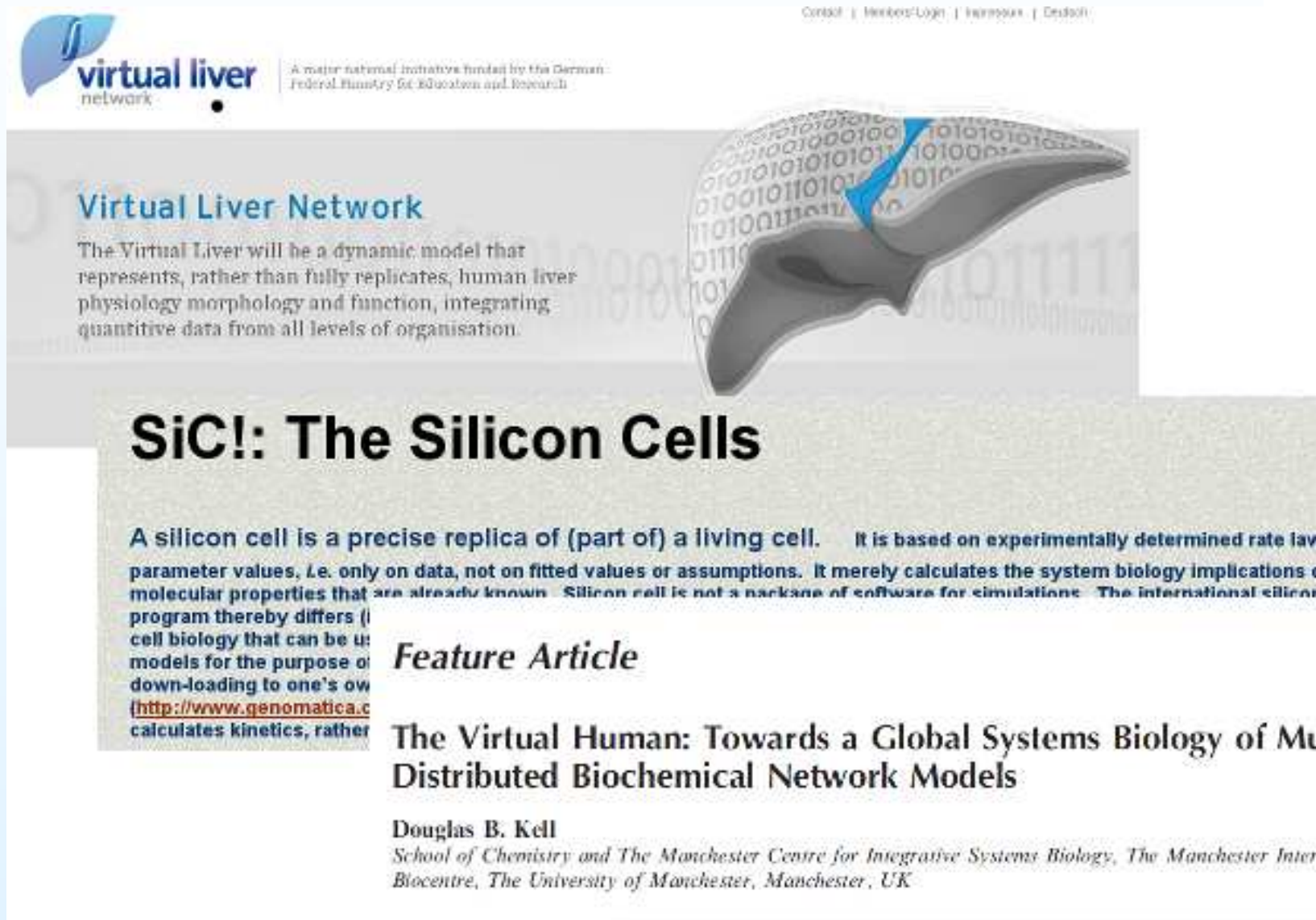
## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- **Virtual Biochemistry**
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary



virtual liver network

A major national initiative funded by the German Federal Ministry for Education and Research

Contact | Members/LogIn | Impressum | Datenschutz

## Virtual Liver Network

The Virtual Liver will be a dynamic model that represents, rather than fully replicates, human liver physiology morphology and function, integrating quantitative data from all levels of organisation.

# SiC!: The Silicon Cells

A silicon cell is a precise replica of (part of) a living cell. It is based on experimentally determined rate law parameter values, i.e. only on data, not on fitted values or assumptions. It merely calculates the system biology implications of molecular properties that are already known. Silicon cell is not a package of software for simulations. The international silicon cell program thereby differs (i) from other cell biology that can be used for the purpose of down-loading to one's own computer and (ii) from other models for the purpose of down-loading to one's own computer. The international silicon cell program calculates kinetics, rather than thermodynamics.

## Feature Article

### The Virtual Human: Towards a Global Systems Biology of Multi-Scale Distributed Biochemical Network Models

Douglas B. Kell  
*School of Chemistry and The Manchester Centre for Integrative Systems Biology, The Manchester Interdisciplinary Biocentre, The University of Manchester, Manchester, UK*

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary



# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Why Model Metabolism?

It came first!

- Metabolism is essential: it is a fundamental process of all living organisms, encompassing all the chemical conversions that convert nutrients into new cellular materials and provide energy for other processes such as movement.
- Metabolism can be useful: bread, alcoholic drinks, cheese, yoghurt, monosodium glutamate, biofuels.
- Metabolism can go wrong: single gene metabolic diseases; obesity, diabetes, heart disease, even cancer, are multi-factorial diseases with a metabolic component.
- We understand how the genes encode metabolism. But how do we exploit that understanding to predict metabolic responses?
- Biotechnological applications: for designing metabolic engineering and synthetic biology strategies.
- Another: design of effective drug therapies.
- Other cell processes yield to similar approaches: signal transduction; cell cycle; apoptosis.

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- **Why Model Metabolism?**
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

# Industrial Biotechnology and Synthetic Biology

Targets for biological production of “platform chemicals” (green chemistry):

<b>Chemical</b>	<b>Derivatives</b>	<b>Chemical</b>	<b>Derivatives</b>
Succinate	1,4 butanediol	Isoprene	Synthetic rubber
3-OH propionate	Acrylate	Farnesene	
Itaconic acid	Methylmethacrylate	Glycerol	Propylene glycol
Ethanol	ethylene, biofuel	Sorbitol	
Lactate	Polylactic acid	Xylitol	
Biohydrocarbons	Biofuel	Furfural	

Choi et al, *Metabolic Engineering*, **28**, 223–239 (2015)

Raw materials include: lignocellulosic biomass, starch, syngas and flue gases (CO<sub>2</sub>/CO/H<sub>2</sub> mixtures), methane, CO<sub>2</sub> and light in algae.

# Design Issues in Synthetic Metabolism

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Can matter flow from inputs to the desired product?
- What is the maximum conversion efficiency obtainable?
- Can the host cell cope with the energy and redox demands of production?
- How can losses to unwanted by-products be avoided?
- How can the rate of production be accelerated?

# Design Issues in Synthetic Metabolism

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Can matter flow from inputs to the desired product?
- What is the maximum conversion efficiency obtainable?
- Can the host cell cope with the energy and redox demands of production?
- How can losses to unwanted by-products be avoided?
- How can the rate of production be accelerated?

# Design Issues in Synthetic Metabolism

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Can matter flow from inputs to the desired product?
- What is the maximum conversion efficiency obtainable?
- Can the host cell cope with the energy and redox demands of production?
- How can losses to unwanted by-products be avoided?
- How can the rate of production be accelerated?

# Design Issues in Synthetic Metabolism

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- **Design Issues in Synthetic Metabolism**
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Can matter flow from inputs to the desired product?
- What is the maximum conversion efficiency obtainable?
- Can the host cell cope with the energy and redox demands of production?
- How can losses to unwanted by-products be avoided?
- How can the rate of production be accelerated?

# Design Issues in Synthetic Metabolism

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- **Design Issues in Synthetic Metabolism**
- Aims of Modelling

## Model Formulation

## A little mathematics

## Summary

- Can matter flow from inputs to the desired product?
- What is the maximum conversion efficiency obtainable?
- Can the host cell cope with the energy and redox demands of production?
- How can losses to unwanted by-products be avoided?
- How can the rate of production be accelerated?



# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.

# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.
- Testing conceptual understanding and extant knowledge in a formal, mathematical framework.

# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.
- Testing conceptual understanding and extant knowledge in a formal, mathematical framework.
- Integration of different types of data and observations in a single framework.

# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.
- Testing conceptual understanding and extant knowledge in a formal, mathematical framework.
- Integration of different types of data and observations in a single framework.
- Generating hypotheses for testing.

# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.
- Testing conceptual understanding and extant knowledge in a formal, mathematical framework.
- Integration of different types of data and observations in a single framework.
- Generating hypotheses for testing.
- Designing experiments *in silico*.

# Aims of Modelling

## Preamble

- Complicated or Complex?
- Modelling and Simulation
- Simulated Life
- Virtual Biochemistry
- Why Model Metabolism?
- Industrial Biotechnology and Synthetic Biology
- Design Issues in Synthetic Metabolism
- **Aims of Modelling**

## Model Formulation

## A little mathematics

## Summary

- Not primarily prediction.
- Testing conceptual understanding and extant knowledge in a formal, mathematical framework.
- Integration of different types of data and observations in a single framework.
- Generating hypotheses for testing.
- Designing experiments *in silico*.
- As models are simplifications, they have to be designed for the specific aims.

Preamble

Model Formulation

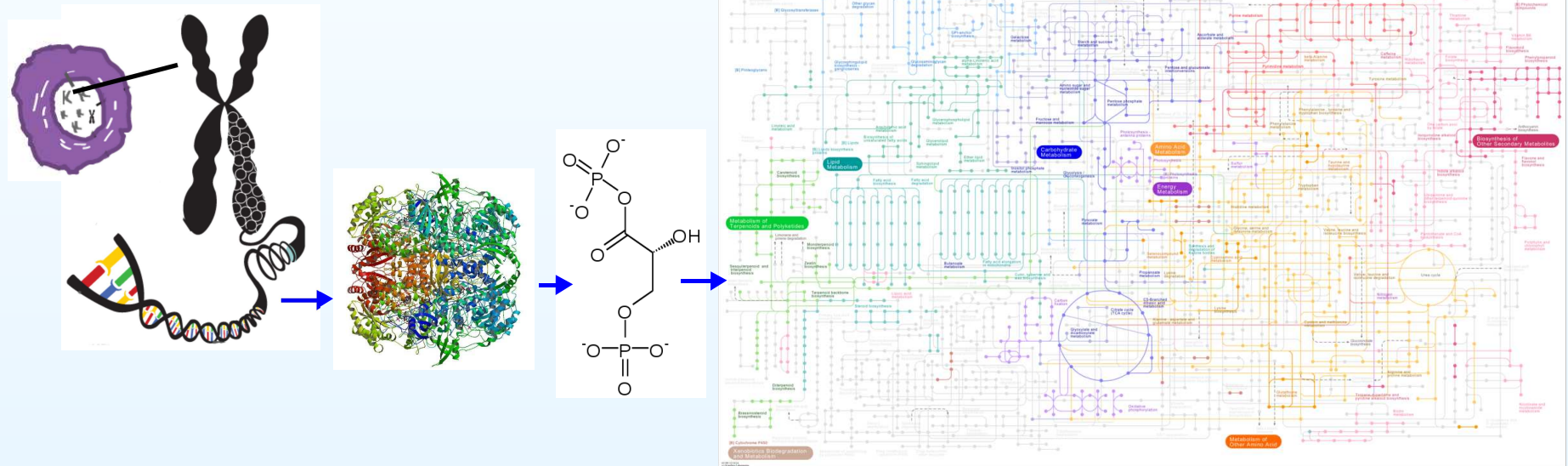
- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic ‘Pathway’
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

A little mathematics

Summary

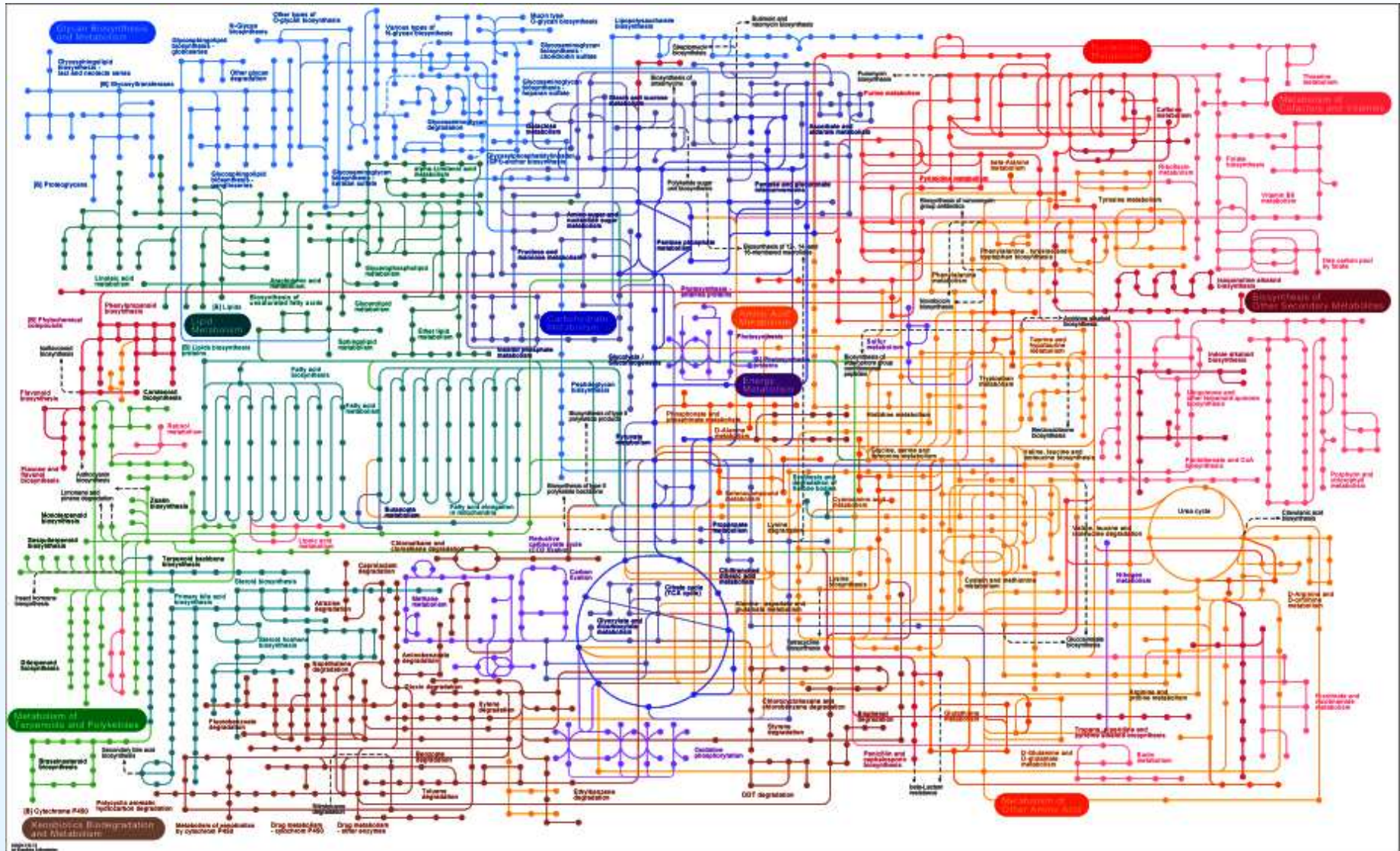
# Model Formulation

# Genotype to Metabolic Phenotype

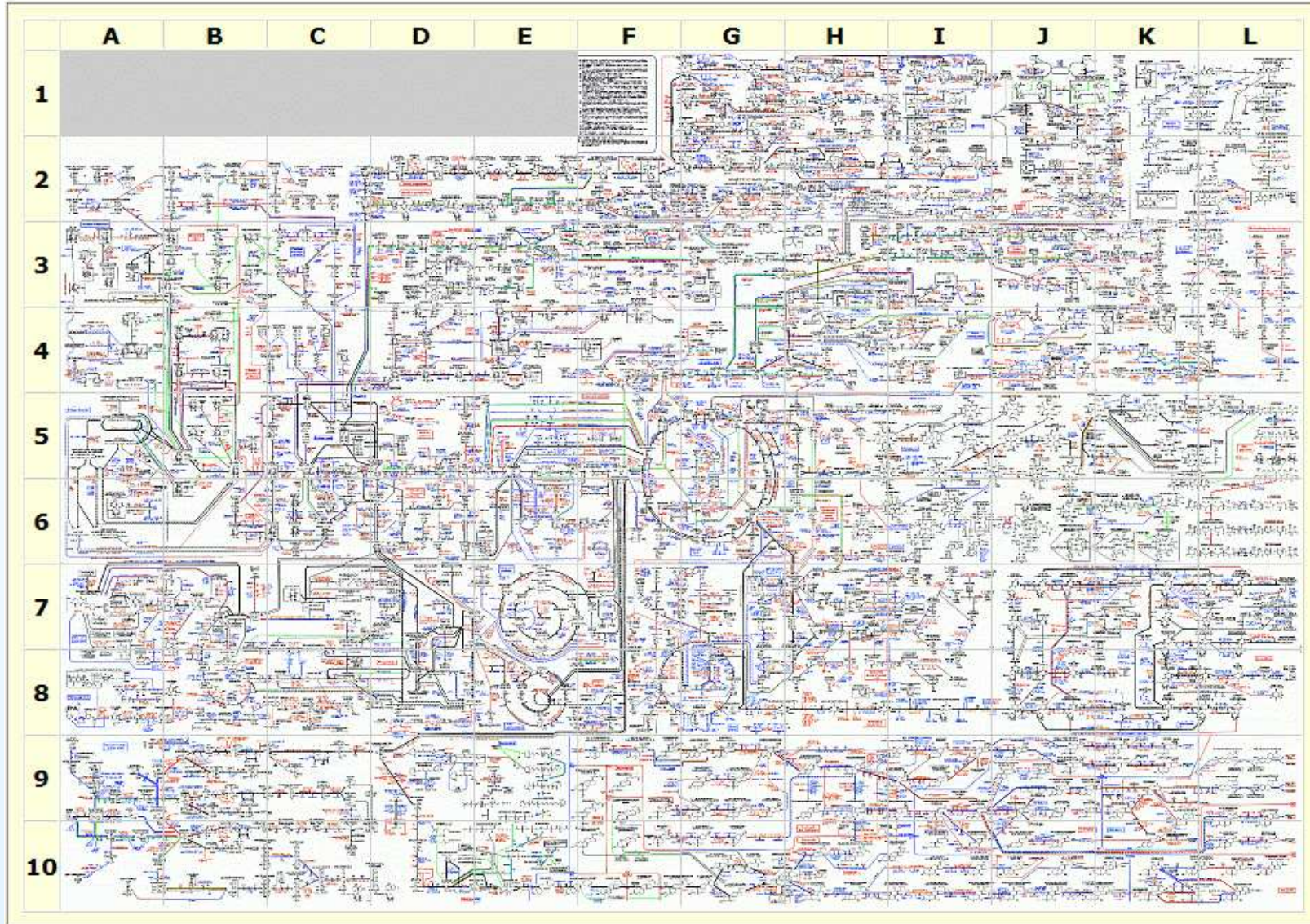




# The Metabolic Network



# The Metabolic Network — More Detail



From Expaty Biochemical Pathways: <http://www.expasy.ch/cgi-bin/search-biochem-index>

# The Metabolic Network — Zoom in

## Preamble

### Model Formulation

- Genotype to Metabolic Phenotype

- The Metabolic Network

- The Metabolic Network — More Detail

- **The Metabolic Network — Zoom in**

- A Metabolic 'Pathway'

- Michaelis–Menten Enzyme Kinetics

- The Reversible M–M Eqn.

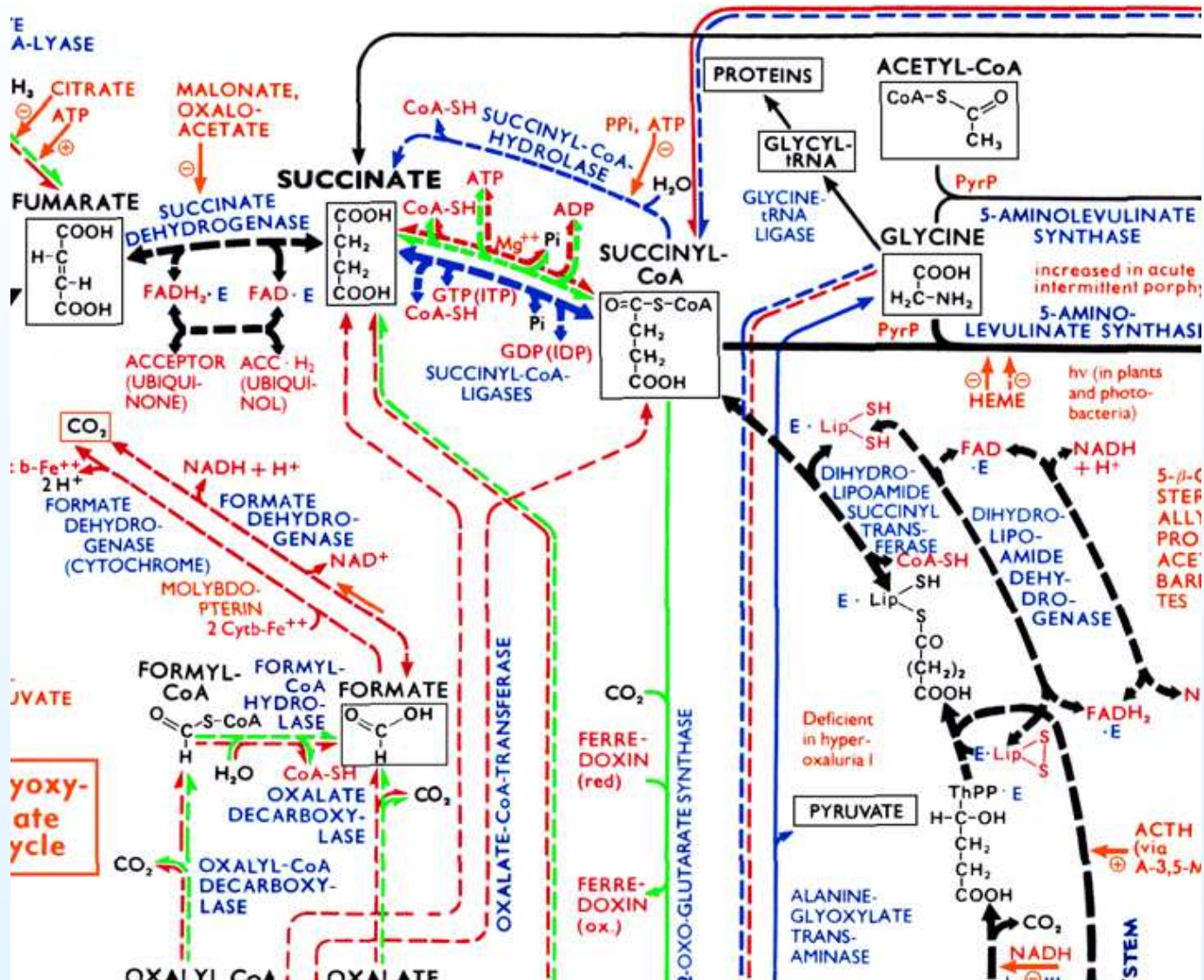
- Steady State

- External and Internal Metabolites

- Summary of Types of Metabolic Model

## A little mathematics

## Summary



From ExPASy Biochemical Pathways: <http://www.expasy.ch/cgi-bin/search-biochem-index>

# A Metabolic 'Pathway'

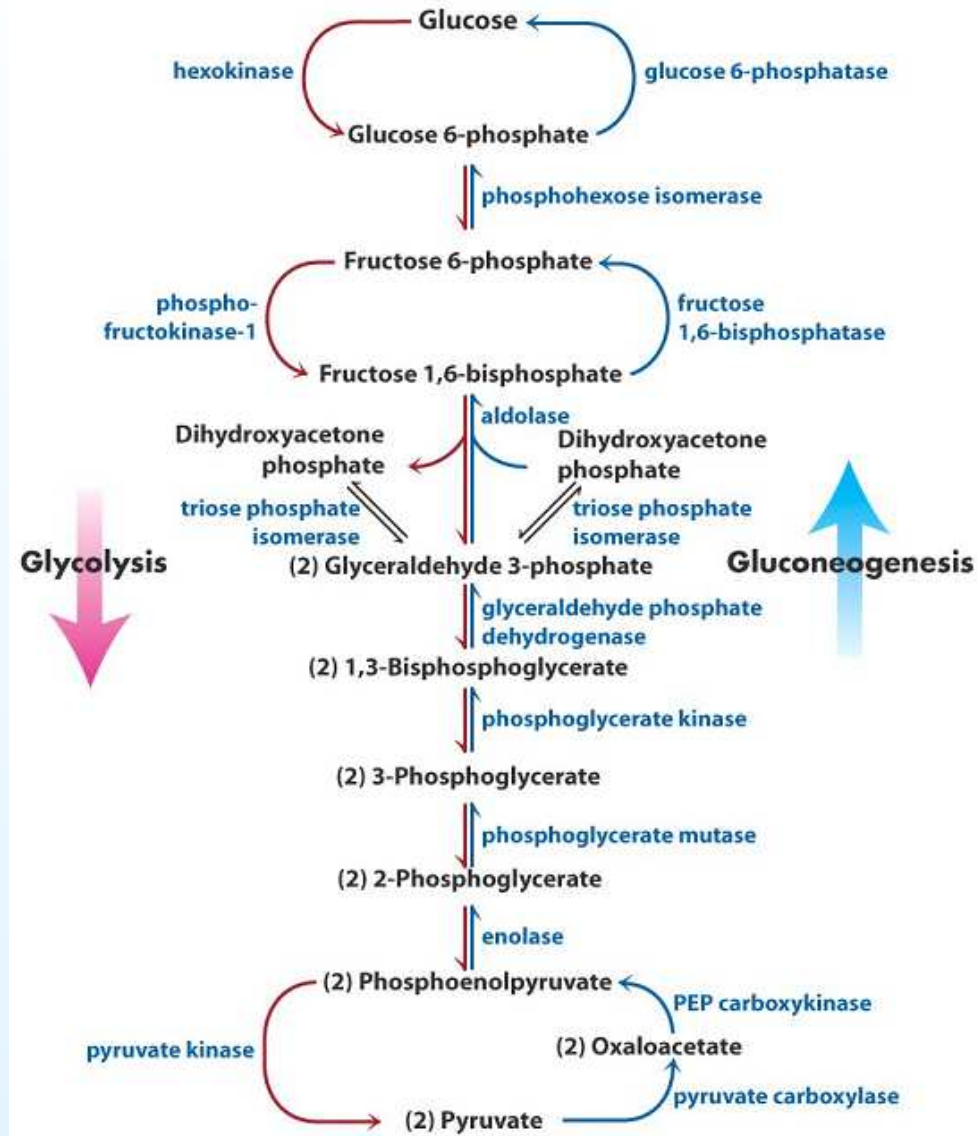
## Preamble

## Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- **A Metabolic 'Pathway'**
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

## A little mathematics

## Summary



From Nelson & Cox, Lehninger's Biochemistry, 4th ed.

# Michaelis–Menten Enzyme Kinetics

## Preamble

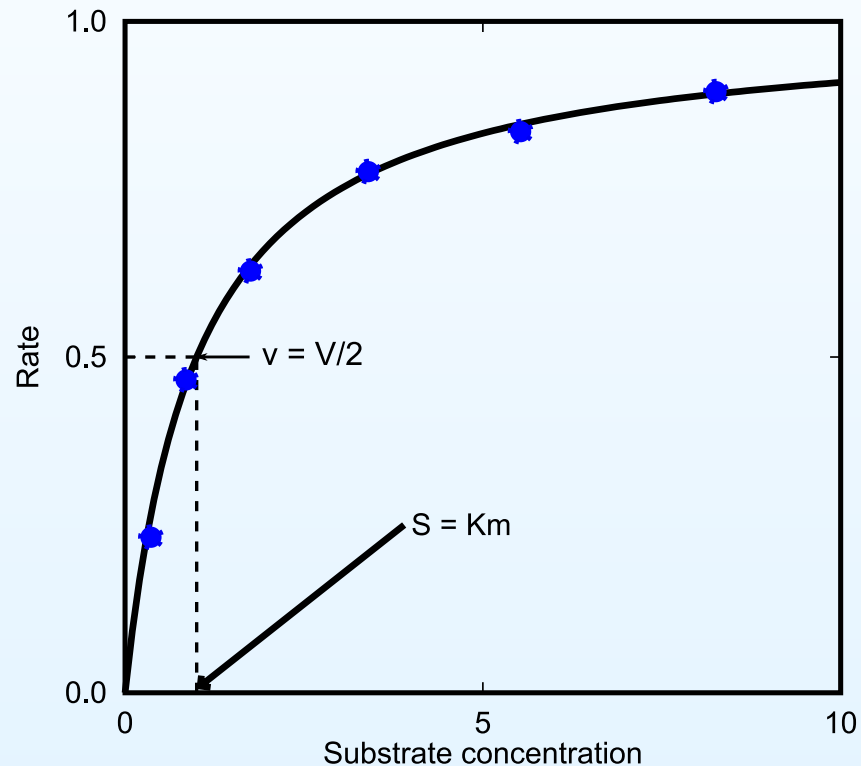
## Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic ‘Pathway’
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

## A little mathematics

## Summary

$$v = \frac{SV}{S + K_m} \quad \text{or} \quad v = f(S)$$



The  $K_m$  and  $V$  have arbitrarily been set to 1, where  $V$  is the *limiting rate* (or maximum velocity,  $V_m$ ) and  $K_m$  is the *Michaelis constant*.

# The Reversible M–M Eqn.

Preamble

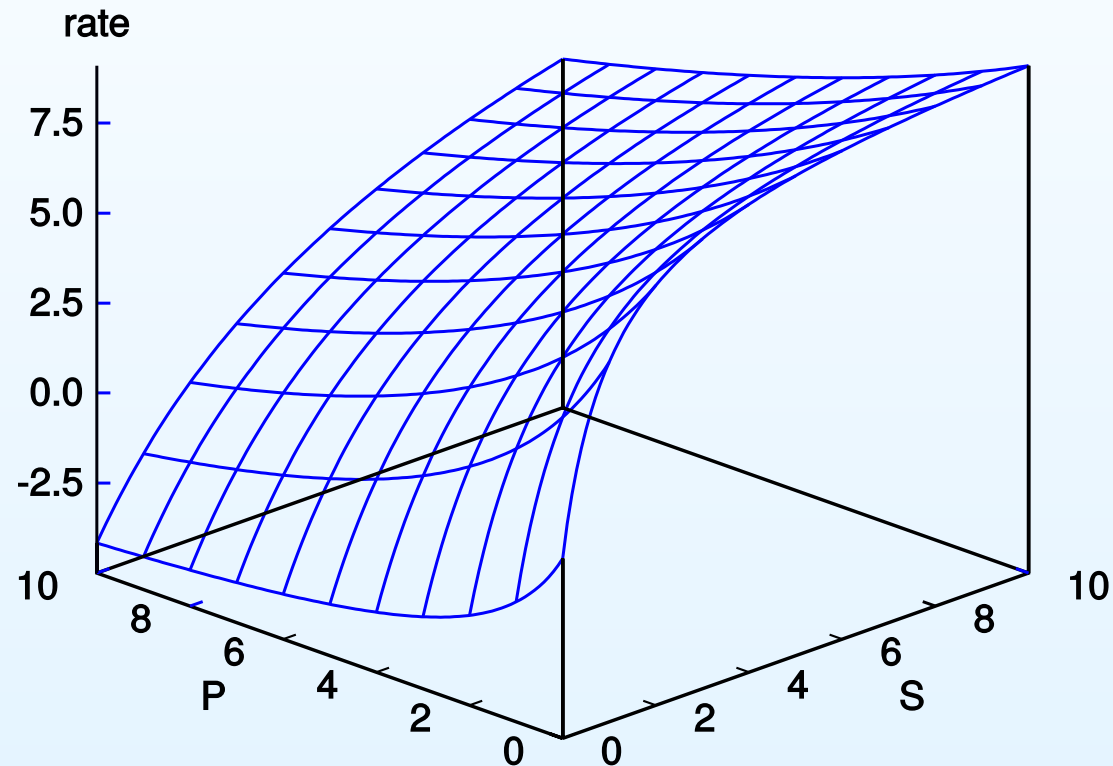
Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic ‘Pathway’
- Michaelis–Menten Enzyme Kinetics
- **The Reversible M–M Eqn.**
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

A little mathematics

Summary

$$v_{net} = \frac{(V_f/K_{m,S})(S - P/K_{eq})}{1 + S/K_{m,S} + P/K_{m,P}} \quad \text{or} \quad v = f(S, P)$$



Simultaneous dependence of enzyme rate on both substrate and product. The parameters have been set to:  $K_{m,S} = 1$ ;

$V_{m,f} = 10$ ;  $K_{m,P} = 2$ , and  $K_{eq} = 4$ .

# Steady State

## Preamble

### Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic ‘Pathway’
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- **Steady State**
- External and Internal Metabolites
- Summary of Types of Metabolic Model

## A little mathematics

## Summary

In a metabolic network there is a flow of matter from the *source* to the *sink*. At steady state, the concentrations of the intermediates remain constant because their rates of formation exactly equal their rates of degradation. The flow through the pathway also remains constant.

If there are very slow changes in the concentrations of metabolites, or the pathway flux, because of slow changes in the source or sink, the pathway may be regarded as being in *quasi steady state* provided the time scale of the changes is very much longer than the time taken by the pathway to approach steady state.

# External and Internal Metabolites

## Preamble

## Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic 'Pathway'
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

## A little mathematics

## Summary

- The source and sink are instances of **external** metabolites in a model: those whose effective concentration is not appreciably modified by metabolic system.



# External and Internal Metabolites

## Preamble

### Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic 'Pathway'
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- **External and Internal Metabolites**
- Summary of Types of Metabolic Model

## A little mathematics

## Summary

- The source and sink are instances of **external** metabolites in a model: those whose effective concentration is not appreciably modified by metabolic system.
- Though extracellular metabolites may be external on account of the extracellular space being larger than the intracellular, some external metabolites can be intracellular.

## Preamble

---

## Model Formulation

---

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic ‘Pathway’
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- **External and Internal Metabolites**
- Summary of Types of Metabolic Model

## A little mathematics

---

## Summary

---

# External and Internal Metabolites

---

- The source and sink are instances of **external** metabolites in a model: those whose effective concentration is not appreciably modified by metabolic system.
- Though extracellular metabolites may be external on account of the extracellular space being larger than the intracellular, some external metabolites can be intracellular.
- Examples include lipid droplets and starch granules that are only slowly depleted.

## Preamble

---

## Model Formulation

---

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic 'Pathway'
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- **External and Internal Metabolites**
- Summary of Types of Metabolic Model

## A little mathematics

---

## Summary

---

# External and Internal Metabolites

---

- The source and sink are instances of **external** metabolites in a model: those whose effective concentration is not appreciably modified by metabolic system.
- Though extracellular metabolites may be external on account of the extracellular space being larger than the intracellular, some external metabolites can be intracellular.
- Examples include lipid droplets and starch granules that are only slowly depleted.
- **Internal** metabolites are those whose concentrations respond to the balance of formation and consumption and therefore are the variables of a metabolic model.

## Preamble

---

## Model Formulation

---

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic 'Pathway'
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- **External and Internal Metabolites**
- Summary of Types of Metabolic Model

## A little mathematics

---

## Summary

---

# External and Internal Metabolites

---

- The source and sink are instances of **external** metabolites in a model: those whose effective concentration is not appreciably modified by metabolic system.
- Though extracellular metabolites may be external on account of the extracellular space being larger than the intracellular, some external metabolites can be intracellular.
- Examples include lipid droplets and starch granules that are only slowly depleted.
- **Internal** metabolites are those whose concentrations respond to the balance of formation and consumption and therefore are the variables of a metabolic model.
- Most intracellular metabolites of a model will count as internal, but it is not impossible for an extracellular metabolite to be internal to the model.

# Summary of Types of Metabolic Model

## Preamble

## Model Formulation

- Genotype to Metabolic Phenotype
- The Metabolic Network
- The Metabolic Network — More Detail
- The Metabolic Network — Zoom in
- A Metabolic 'Pathway'
- Michaelis–Menten Enzyme Kinetics
- The Reversible M–M Eqn.
- Steady State
- External and Internal Metabolites
- Summary of Types of Metabolic Model

## A little mathematics

## Summary

- **Structural** — needs reaction list; gives existence and number of routes; optimal stoichiometries; network flux values.
- **Dynamic or Kinetic** — needs full kinetic description of each enzyme/step; predicts time–courses, steady–states, sensitivity analysis or control distribution . . . Can be deterministic or stochastic.
- **Sensitivity analysis / Control analysis / S–systems** — needs effective kinetics near steady–state; predicts control distribution, response of steady state to perturbations.

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of Structural Analysis

- Structural Analysis Methods

- Aren't Graph

Algorithms the Answer?

Summary

# A little mathematics

# Reaction Network to Mathematical Object

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

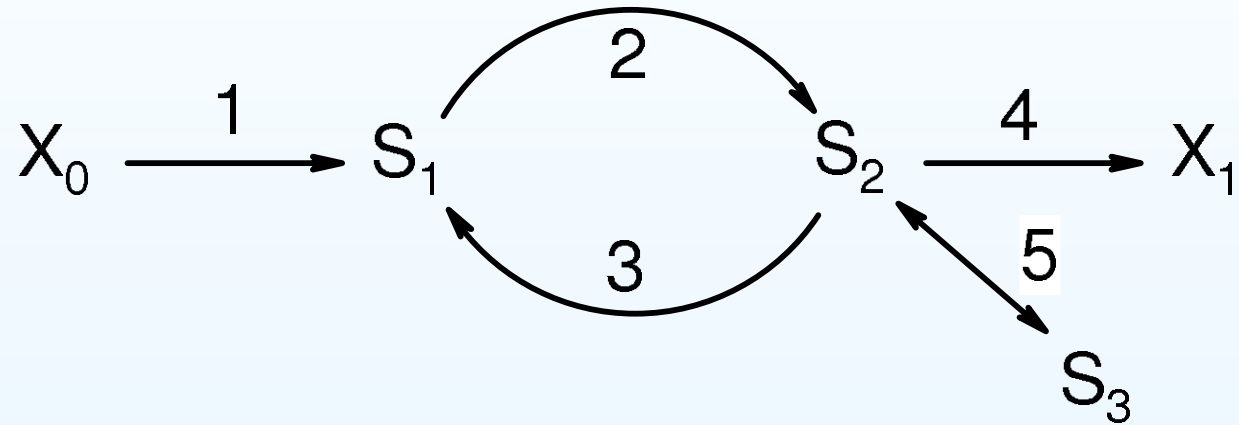
Methods

● Aren't Graph

Algorithms the Answer?

Summary

Consider a simple metabolic network, e.g.:



# Reaction Network to Mathematical Object

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

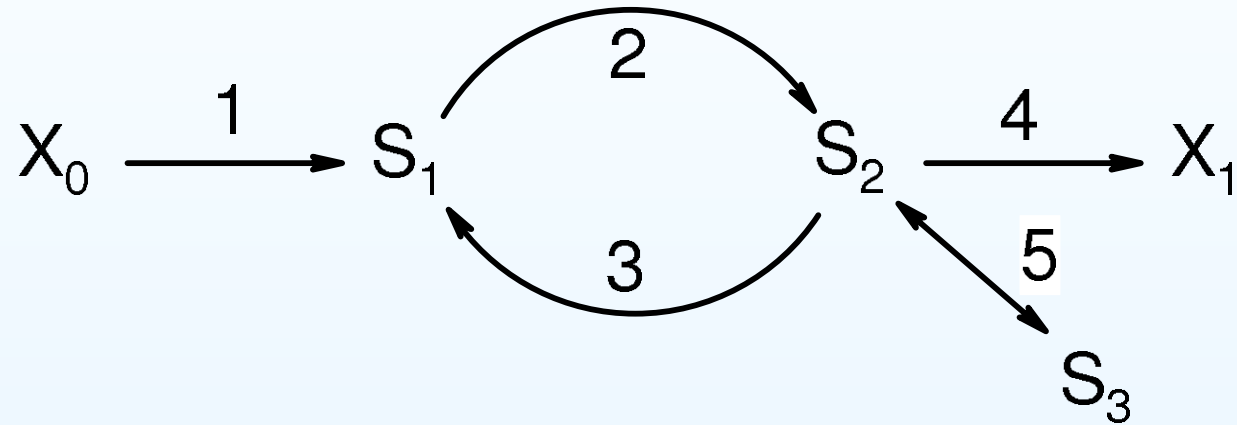
Methods

● Aren't Graph

Algorithms the Answer?

Summary

Consider a simple metabolic network, e.g.:



r1:  $X_0 \rightarrow S_1 \sim$

r2:  $S_1 \rightarrow S_2 \sim$

r3:  $S_2 \rightarrow S_1 \sim$

r4:  $S_2 \rightarrow X_1 \sim$

r5:  $S_2 \leftrightarrow S_3 \sim$



# Reaction Network to Mathematical Object

Preamble

Model Formulation

A little mathematics

● Reaction Network to Mathematical Object

● Kinetics of the Metabolites

● Separation of Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

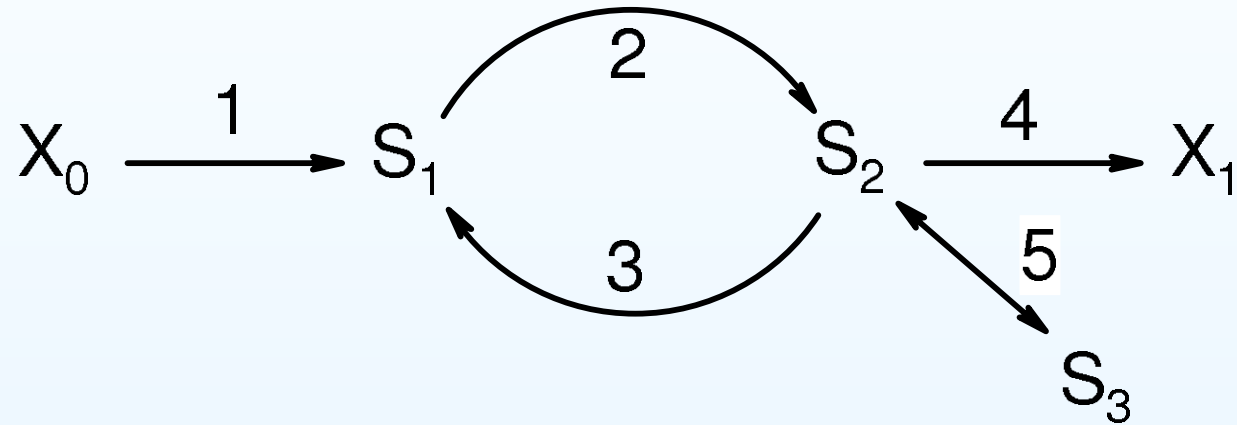
Methods

● Aren't Graph

Algorithms the Answer?

Summary

Consider a simple metabolic network, e.g.:



r1:  $X_0 \rightarrow S_1 \sim$

r2:  $S_1 \rightarrow S_2 \sim$

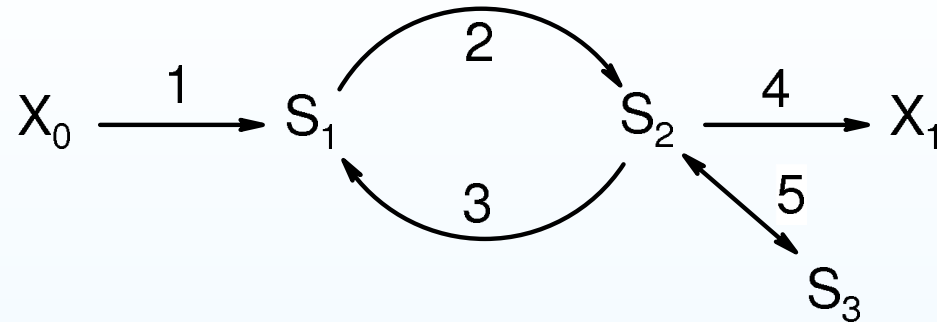
r3:  $S_2 \rightarrow S_1 \sim$

r4:  $S_2 \rightarrow X_1 \sim$

r5:  $S_2 \leftrightarrow S_3 \sim$

	r1	r2	r3	r4	r5
$S_1$	1	-1	1	0	0
$S_2$	0	1	-1	-1	-1
$S_3$	0	0	0	0	1

# Kinetics of the Metabolites



By inspection of the diagram:

$$\frac{dS_1}{dt} = v_1 - v_2 + v_3$$

$$\frac{dS_2}{dt} = v_2 - v_3 - v_4 - v_5$$

$$\frac{dS_3}{dt} = v_5$$

How can we generalize this?

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics
- Steady State Structural Modelling

- Advantages of Structural Analysis Methods

- Aren't Graph Algorithms the Answer?

Summary

## Separation of Structure and Kinetics

The rate at which the substrate concentrations are changing is given by  $\mathbf{N} \cdot \mathbf{v}$ , where  $\mathbf{N}$  is the stoichiometry matrix, and  $\mathbf{v}$  is a vector of enzyme kinetic functions. So for our substrate cycle network:

$$\begin{bmatrix} \frac{dS_1}{dt} \\ \frac{dS_2}{dt} \\ \frac{dS_3}{dt} \end{bmatrix} = \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

Methods

● Aren't Graph

Algorithms the Answer?

Summary

## Separation of Structure and Kinetics

The rate at which the substrate concentrations are changing is given by  $\mathbf{N} \cdot \mathbf{v}$ , where  $\mathbf{N}$  is the stoichiometry matrix, and  $\mathbf{v}$  is a vector of enzyme kinetic functions. So for our substrate cycle network:

$$\begin{bmatrix} \frac{dS_1}{dt} \\ \frac{dS_2}{dt} \\ \frac{dS_3}{dt} \end{bmatrix} = \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

where each  $v_i$  is the rate function for enzyme  $i$ , depending on the variable metabolites and the parameters  $V_{m,i}$ ,  $K_{m,i}$  etc, as  $f_i(\mathbf{S})$ .

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

Methods

● Aren't Graph

Algorithms the Answer?

Summary

## Separation of Structure and Kinetics

The rate at which the substrate concentrations are changing is given by  $\mathbf{N} \cdot \mathbf{v}$ , where  $\mathbf{N}$  is the stoichiometry matrix, and  $\mathbf{v}$  is a vector of enzyme kinetic functions. So for our substrate cycle network:

$$\begin{bmatrix} \frac{dS_1}{dt} \\ \frac{dS_2}{dt} \\ \frac{dS_3}{dt} \end{bmatrix} = \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

where each  $v_i$  is the rate function for enzyme  $i$ , depending on the variable metabolites and the parameters  $V_{m,i}$ ,  $K_{m,i}$  etc, as  $f_i(\mathbf{S})$ .

Integrating this set of non-linear differential equations gives a **dynamic model** of our network.

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

Methods

● Aren't Graph

Algorithms the Answer?

Summary

## Separation of Structure and Kinetics

The rate at which the substrate concentrations are changing is given by  $\mathbf{N} \cdot \mathbf{v}$ , where  $\mathbf{N}$  is the stoichiometry matrix, and  $\mathbf{v}$  is a vector of enzyme kinetic functions. So for our substrate cycle network:

$$\begin{bmatrix} \frac{dS_1}{dt} \\ \frac{dS_2}{dt} \\ \frac{dS_3}{dt} \end{bmatrix} = \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

where each  $v_i$  is the rate function for enzyme  $i$ , depending on the variable metabolites and the parameters  $V_{m,i}$ ,  $K_{m,i}$  etc, as  $f_i(\mathbf{S})$ .

Integrating this set of non-linear differential equations gives a **dynamic model** of our network.

The steady state is a set of non-linear simultaneous equations that can be solved for the steady state values of  $\mathbf{S}$ .

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● Steady State

Structural Modelling

● Advantages of

Structural Analysis

● Structural Analysis

Methods

● Aren't Graph

Algorithms the Answer?

Summary

# Steady State Structural Modelling

Preamble

Model Formulation

A little mathematics

● Reaction Network to  
Mathematical Object

● Kinetics of the  
Metabolites

● Separation of  
Structure and Kinetics

● **Steady State  
Structural Modelling**

● Advantages of  
Structural Analysis

● Structural Analysis  
Methods

● Aren't Graph  
Algorithms the Answer?

Summary

Any metabolic network at steady state satisfies the relationship  $\mathbf{N} \cdot \mathbf{v} = \mathbf{0}$ , where  $\mathbf{N}$  is the stoichiometry matrix, exemplified by our model network:

$$\begin{matrix} S_1 \\ S_2 \\ S_3 \end{matrix} \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

# Steady State Structural Modelling

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- **Steady State Structural Modelling**

- Advantages of Structural Analysis

- Structural Analysis Methods

- Aren't Graph

Algorithms the Answer?

Summary

Any metabolic network at steady state satisfies the relationship  $\mathbf{N} \cdot \mathbf{v} = \mathbf{0}$ , where  $\mathbf{N}$  is the stoichiometry matrix, exemplified by our model network:

$$\begin{matrix} S_1 \\ S_2 \\ S_3 \end{matrix} \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

Structural modelling involves exploring the solutions of this equation, regarding the  $v_i$  as the unknown variables.



# Steady State Structural Modelling

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- **Steady State Structural Modelling**

- Advantages of Structural Analysis

- Structural Analysis Methods

- Aren't Graph

Algorithms the Answer?

Summary

Any metabolic network at steady state satisfies the relationship  $\mathbf{N} \cdot \mathbf{v} = \mathbf{0}$ , where  $\mathbf{N}$  is the stoichiometry matrix, exemplified by our model network:

$$\begin{matrix} S_1 \\ S_2 \\ S_3 \end{matrix} \begin{bmatrix} 1 & -1 & 1 & 0 & 0 \\ 0 & 1 & -1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \cdot \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

Structural modelling involves exploring the solutions of this equation, regarding the  $v_i$  as the unknown variables.

The equation is linear, but under-determined. Though solutions are not unique, they distinguish between **feasible** and **non-feasible** states of the network.

# Advantages of Structural Analysis

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- **Advantages of Structural Analysis**

- Structural Analysis Methods

- Aren't Graph

Algorithms the Answer?

Summary

- Knowledge is more complete for network structure than for enzyme kinetics.
- Structural analysis involves simple linear equations; dynamic analysis involves non-linear enzyme kinetic functions.
- The network structure places limitations that constrain the network dynamics, irrespective of the kinetics, e.g.:
  - Whether viable routes exist from nutrients to stated metabolic products;
  - Whether some routes remain after deletion (knock-out mutation) of the steps catalysed by a particular enzyme;
  - What the maximum obtainable conversion yield is for formation of any metabolite from a given set of sources, and
- Structural models underlie kinetic models, and other techniques such as Metabolic Flux Analysis and Metabolic Control Analysis.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis**

Methods

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis**

**Methods**

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis Methods**

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis Methods**

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis**

Methods

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis**

Methods

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.



# Structural Analysis Methods

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

Structural Modelling

- Advantages of

Structural Analysis

- **Structural Analysis**

Methods

- Aren't Graph

Algorithms the Answer?

Summary

- Null space vectors *Fell, Palsson et al*
- Computer construction of transformation routes *Serriotsis & Bailey; Mavrovouniotis et al*
- Graph analysis techniques *various*
- Elementary modes *Schuster et al*
- Convex basis / Extreme pathways *Palsson et al*
- Reaction (enzyme) subsets
- Linear programming - single optimal route *Small & Fell, Palsson et al*. Became Flux Balance Analysis and gave rise to genome-scale metabolic modelling.

# Aren't Graph Algorithms the Answer?

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

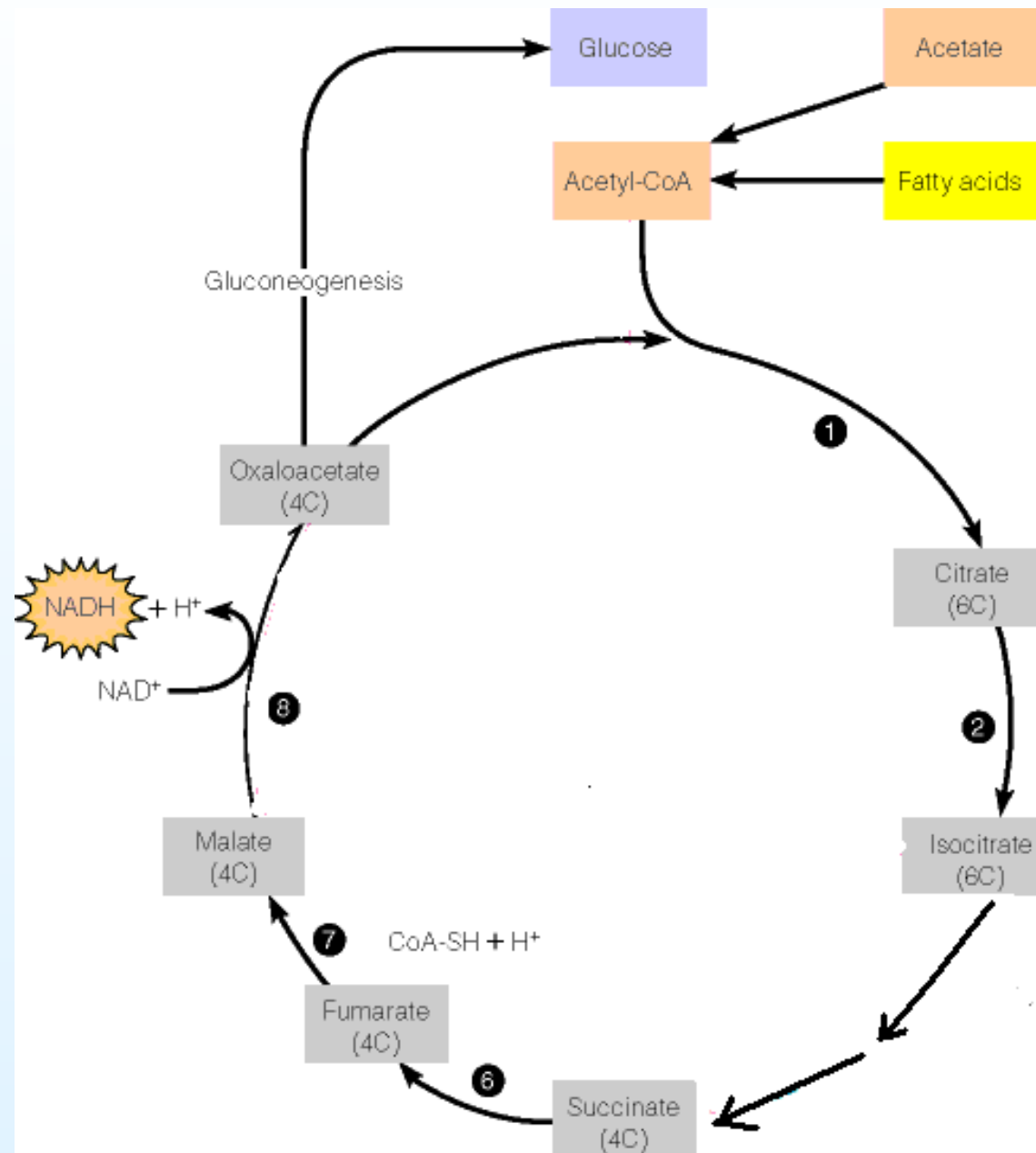
Structural Modelling

- Advantages of Structural Analysis

- Structural Analysis Methods

- Aren't Graph Algorithms the Answer?

Summary



# Aren't Graph Algorithms the Answer?

Preamble

Model Formulation

A little mathematics

- Reaction Network to Mathematical Object

- Kinetics of the Metabolites

- Separation of Structure and Kinetics

- Steady State

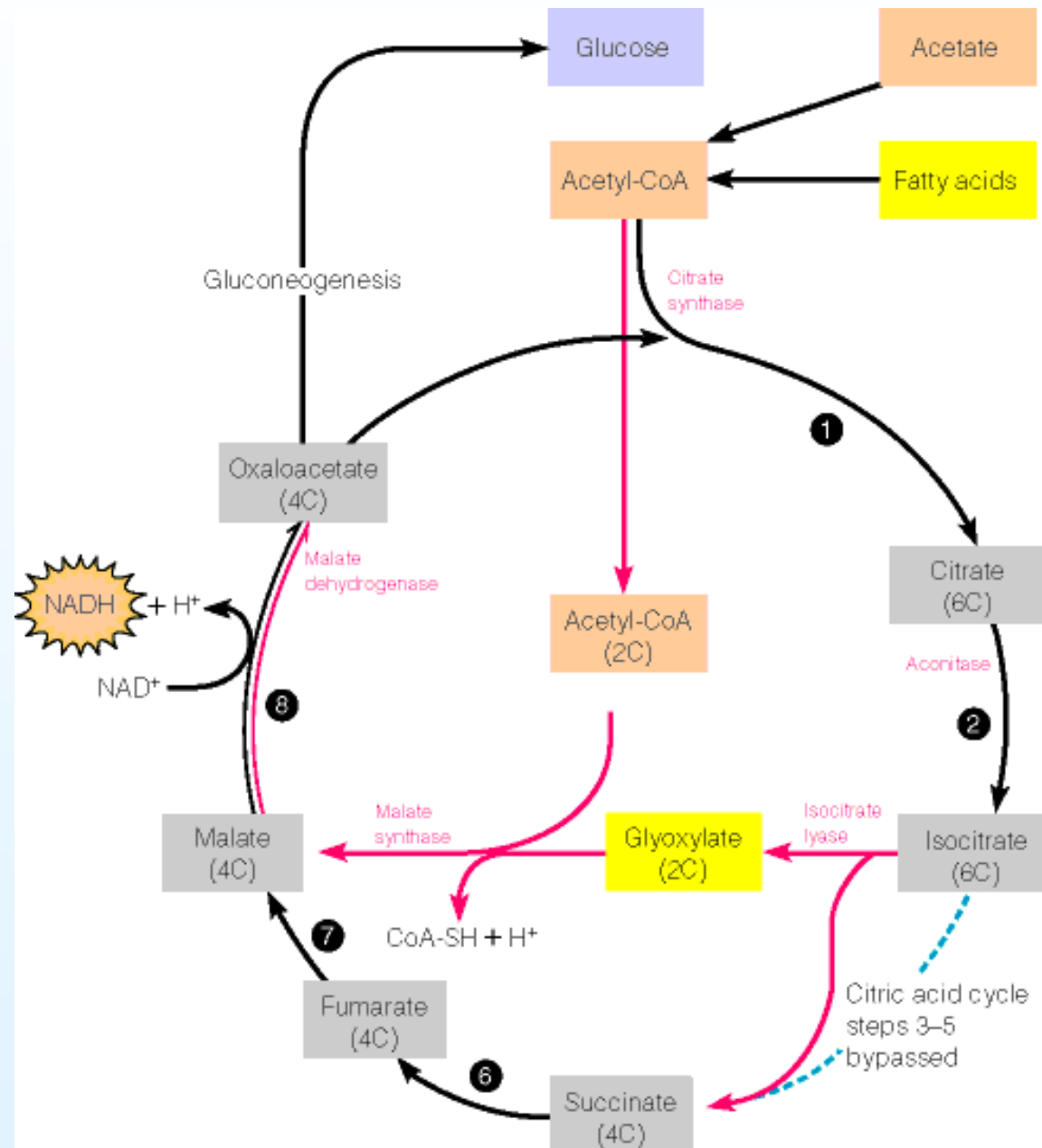
Structural Modelling

- Advantages of Structural Analysis

- Structural Analysis Methods

- Aren't Graph Algorithms the Answer?

Summary



# Summary

Preamble

Model Formulation

A little mathematics

Summary

● **Summary**

- Metabolic modelling is feasible and potentially useful.

# Summary

Preamble

Model Formulation

A little mathematics

Summary

● **Summary**

- Metabolic modelling is feasible and potentially useful.
- Mathematical representation of a metabolic network allows us to separate the network structure and the kinetics.

# Summary

Preamble

Model Formulation

A little mathematics

Summary

● **Summary**

- Metabolic modelling is feasible and potentially useful.
- Mathematical representation of a metabolic network allows us to separate the network structure and the kinetics.
- Network structure places constraints on the feasible behaviour of a network at steady state.

# Summary

Preamble

Model Formulation

A little mathematics

Summary

● **Summary**

- Metabolic modelling is feasible and potentially useful.
- Mathematical representation of a metabolic network allows us to separate the network structure and the kinetics.
- Network structure places constraints on the feasible behaviour of a network at steady state.
- These constraints underlie kinetic models of metabolism.

# Summary

Preamble

Model Formulation

A little mathematics

Summary

● **Summary**

- Metabolic modelling is feasible and potentially useful.
- Mathematical representation of a metabolic network allows us to separate the network structure and the kinetics.
- Network structure places constraints on the feasible behaviour of a network at steady state.
- These constraints underlie kinetic models of metabolism.
- Structural modelling investigates the implications of these network constraints.