

# Modelling and Simulation of Biological Processes

Melanie I Stefan, University of Edinburgh

OIST Collaborative International Undergraduate Workshop

August 2015

# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?
- 3 Introduction to COPASI
- 4 Modelling a biochemical system
- 5 Challenges and Questions around Modelling
- 6 Summary

# Learning Goals

## Thinking

- Reproduce the steps in going from a conceptual model to a computational model
- Discuss the assumptions behind a model
- Recognise a situation where simulations are beneficial

# Learning Goals

## Thinking

- Reproduce the steps in going from a conceptual model to a computational model
- Discuss the assumptions behind a model
- Recognise a situation where simulations are beneficial

## Doing

- Build simple models using the COPASI simulation software
- Navigate BioModels Database

# Learning Goals

## Thinking

- Reproduce the steps in going from a conceptual model to a computational model
- Discuss the assumptions behind a model
- Recognise a situation where simulations are beneficial

## Doing

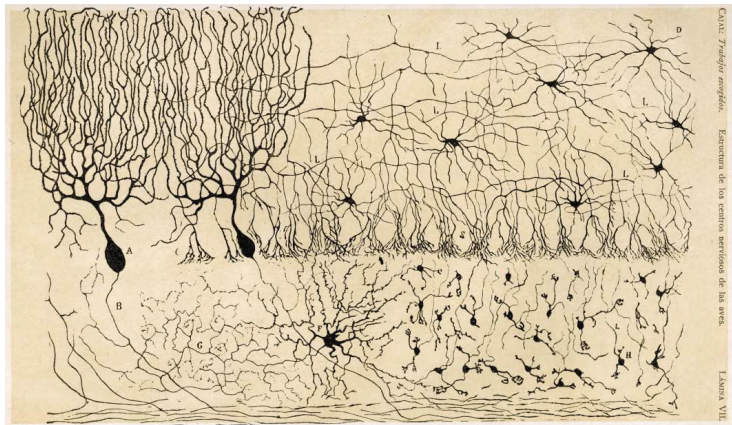
- Build simple models using the COPASI simulation software
- Navigate BioModels Database

## Feeling

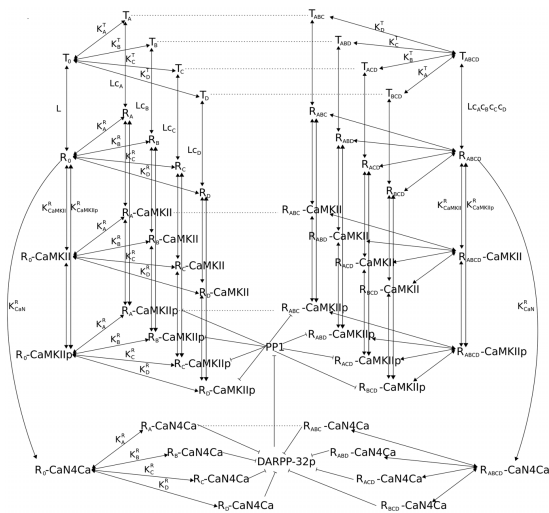
- Appreciate the value of modelling and simulations in biology
- Feel empowered to use simulations in your own work

# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?**
- 3 Introduction to COPASI
- 4 Modelling a biochemical system
- 5 Challenges and Questions around Modelling
- 6 Summary

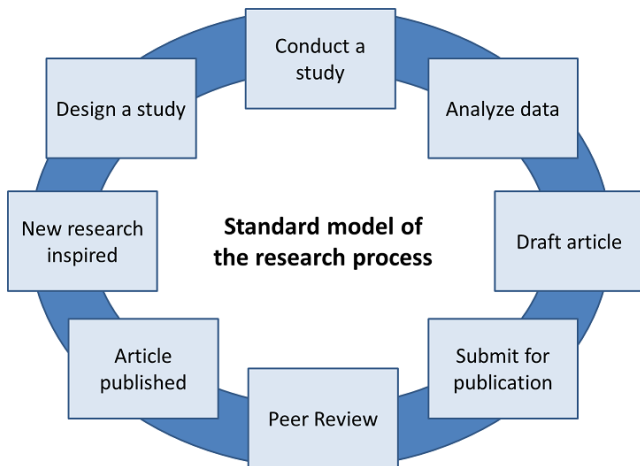


C. Sotelo, *Nat Rev Neurosci* **4**, 71–77 (Jan. 2003)

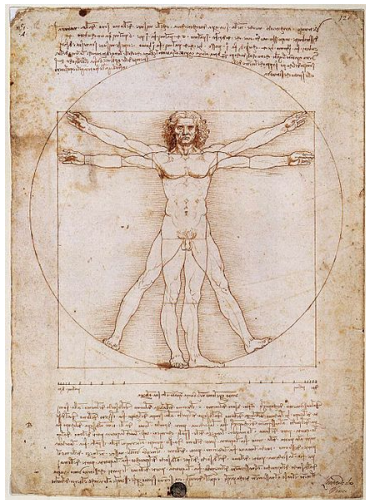


L. Li *et al.*, *PLoS One* 7, e43810 (2012)

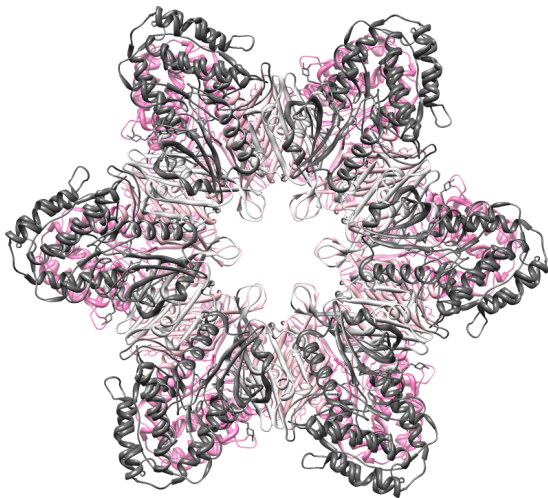




B. Nosek, *Standard model of the research process*, Digital image, 2015



L. Da Vinci, *Vitruvian Man*, Pen, ink, watercolour and metalpoint on paper, 1492



L. H. Chao *et al.*, *Cell* **146**, 732–745 (Sept. 2011)

Molecular graphics produced using Chimera: E. F. Pettersen *et al.*, *J Comput Chem* **25**, 1605–1612 (Oct. 2004)

# What are models and why do we need them?

# What are models and why do we need them?

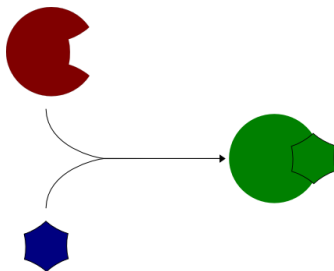
## Uses of computational modelling

- Build intuition
- Building understanding where intuition fails
- Proof-of-concept results
- Suggesting experiments
- Predicting outcomes of mutations/disease/environmental factors

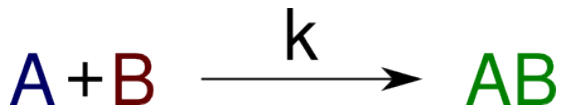
# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?
- 3 Introduction to COPASI**
- 4 Modelling a biochemical system
- 5 Challenges and Questions around Modelling
- 6 Summary

# What are we interested in?



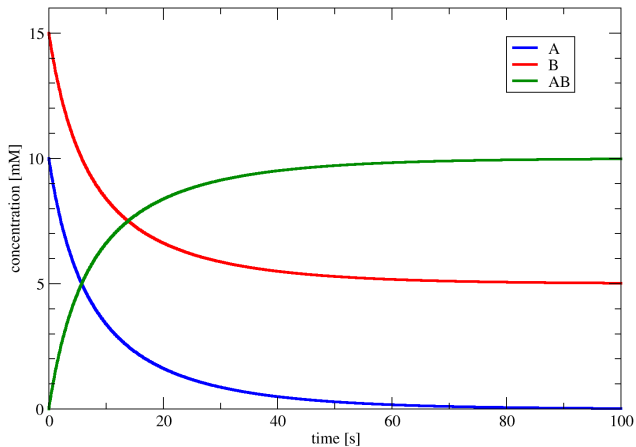
# What are we interested in?





# What are we interested in?

## Formation of AB complex



# Meet COPASI

## COPASI Basics

- CComplex PATHway Simulator
- [http://www.copasi.org/tiki-view\\_articles.php](http://www.copasi.org/tiki-view_articles.php)

S. Hoops *et al.*, *Bioinformatics* **22**, 3067–3074 (Dec. 2006)

# Parts of a COPASI model

## Model specification

- Parts (molecules, compartments, etc.)
- Parameters (reaction rates, initial concentrations, ...)
- Interactions (reactions, rules, ...)

# Parts of a COPASI model

## Model specification

- Parts (molecules, compartments, etc.)
- Parameters (reaction rates, initial concentrations, ...)
- Interactions (reactions, rules, ...)

## Simulation

- Output (parameters to track, plots, ...)
- Task (time course, parameter scan, optimisation, ...)
- Simulation parameters (e.g. length of time course)

# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?
- 3 Introduction to COPASI
- 4 Modelling a biochemical system**
- 5 Challenges and Questions around Modelling
- 6 Summary

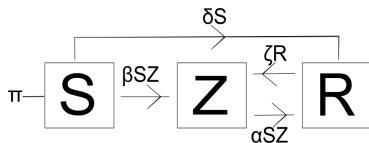
# In-class exercise: Drug-receptor interaction

- Install Copasi
- Work on Exercise 1 (Drug binding)
- If you are done or get bored, work on Exercise 2 (Mystery Model)

# Do all models have to be biochemical?

# Do all models have to be biochemical?

Zombie attack model:



P. Munz *et al.*, In: J.M. Tchenche and C. Chiyaka, editors, *Infectious Disease Modelling Research Progress* (Nova Science, 2009), pp. 133–150



# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?
- 3 Introduction to COPASI
- 4 Modelling a biochemical system
- 5 Challenges and Questions around Modelling**
- 6 Summary

# Challenges and Problems

What problems do we face when modelling?

# Challenges and Problems

What problems do we face when modelling?

- Validation, falsification
- Estimating parameters, constraining the model
- Experimental limits
- Complex models: space, multiple states etc.
- Data sharing and reproducibility

# BioModels Database

The screenshot shows the BioModels Database website. At the top, there is a navigation bar with links for Databases, Tools, Research, Training, Industry, About Us, and Help. Below this is a secondary navigation bar with links for BioModels Home, Models, Submit, Support, About BioModels, and Contact us. The main content area includes a search bar with a 'Find' button and a 'Help/Feedback' link. The page is divided into several sections:

- Browse models:** Contains links for 'Curated models (409)', 'Browse models using GO', and 'Non-curated models (420)'.
- Simulate in JWS Online:** A link to simulate models.
- Submit a model:** A link to submit new models.
- Links:** A list of links including 'Main Instance at EMBL-EBL, UK', 'Mirror at Caltech, USA', 'Project on SourceForge', 'Web Services', and 'Download archived models'.
- Model of the month:** A section highlighting a specific model, 'February 2012: A deterministic modeling of the dynamic biotransformation and transport processes of Abiraterone...'. It includes a diagram of a metabolic pathway.
- News:** A section with recent updates, including '20th February 2010: Twenty-first Release of BioModels Database!' and '19 April 2011: Nineteenth Release!'.

<http://www.ebi.ac.uk/biomodels-main/>  
 C. Li et al., *BMC Syst Biol* 4, 92 (2010)

# BioModels Database

Work on Exercise 3

# Outline

- 1 Learning Goals
- 2 What are models and why do we need them?
- 3 Introduction to COPASI
- 4 Modelling a biochemical system
- 5 Challenges and Questions around Modelling
- 6 Summary**

<http://answergarden.ch/view/182197>

## References I

C. Sotelo, *Nat Rev Neurosci* **4**, 71–77 (Jan. 2003).

L. Li, M. I. Stefan, N. Le Novère, *PLoS One* **7**, e43810 (2012).

B. Nosek, *Standard model of the research process*, Digital image, 2015, <http://projectimplicit.net/nosek/interests.htm>.

L. Da Vinci, *Vitruvian Man*, Pen, ink, watercolour and metalpoint on paper, 1492,  
<https://commons.wikimedia.org/wiki/File:Vitruvian.jpg>.

L. H. Chao *et al.*, *Cell* **146**, 732–745 (Sept. 2011).

E. F. Pettersen *et al.*, *J Comput Chem* **25**, 1605–1612 (Oct. 2004).

S. Hoops *et al.*, *Bioinformatics* **22**, 3067–3074 (Dec. 2006).



## References II

P. Munz, I. Hudea, J. Imad, R. J. Smith, *In: J.M. Tchuente and C. Chiyaka, editors, Infectious Disease Modelling Research Progress* (Nova Science, 2009), pp. 133–150.

C. Li *et al.*, *BMC Syst Biol* **4**, 92 (2010).