## Modelling and Simulation of Biological Processes

#### Melanie I Stefan, University of Edinburgh

OIST Collaborative International Undergraduate Workshop

August 2015

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## Outline

### 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

#### 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

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#### Doing

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- Navigate BioModels Database

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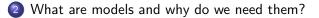
### Feeling

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

Modelling and Simulation

## Outline

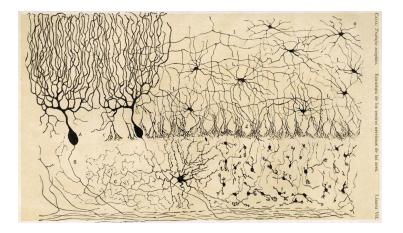
#### Learning Goals



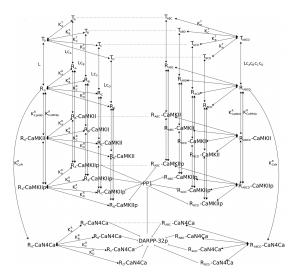
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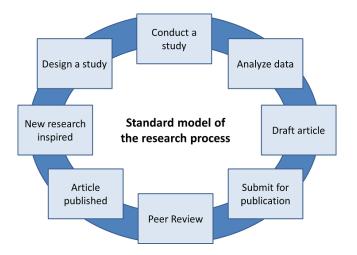


C. Sotelo, Nat Rev Neurosci 4, 71-77 (Jan. 2003)

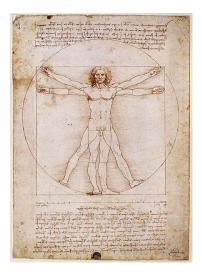


L. Li et al., PLoS One 7, e43810 (2012)

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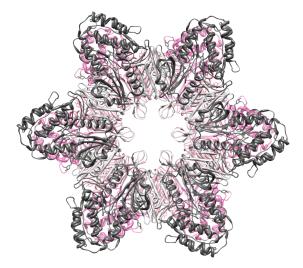
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L. Da Vinci, *Vitruvian Man*, Pen, ink, watercolour and metalpoint on paper, 1492

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Modelling and Simulation



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)

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Modelling and Simulation

## What are models and why do we need them?

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#### 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

#### Learning Goals

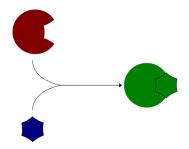
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## What are we interested in?

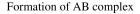


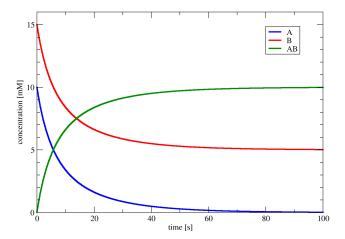
## What are we interested in?

# $A+B \xrightarrow{k} AB$

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## What are we interested in?





## Meet COPASI

#### **COPASI** Basics

- COmplex PAthway SImulator
- http://www.copasi.org/tiki-view\_articles.php
- S. Hoops et al., Bioinformatics 22, 3067-3074 (Dec. 2006)

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## Parts of a COPASI model

#### Model specification

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

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#### Simulation

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

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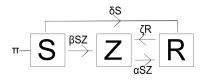
## In-class exercise: Drug-receptor interaction

- 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?

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Zombie attack model:



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

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## **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

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

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## **BioModels** Database

Work on Exercise 3

## Outline

- Modelling a biochemical system



### Summary

#### http://answergarden.ch/view/182197

- 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).
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