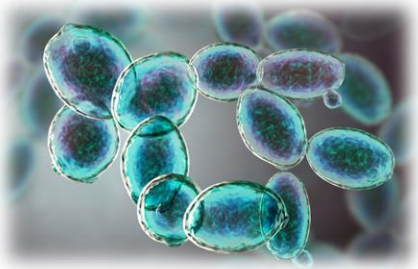
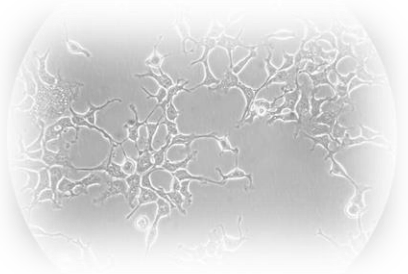
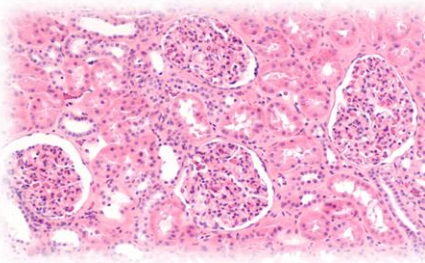


Modelling human disease

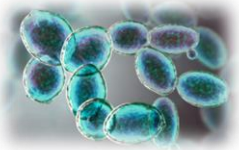
from fruit flies to sea urchins





What does modelling actually mean?

A biological model is an organism or system representing a more complex biological entity.



These can be:

- Mathematical models
- *In vitro* models
- Animal models
- Plant models
- Bacteria/single celled organisms

That recreate aspects of human tissue function or disease.

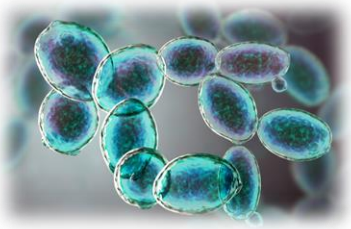
Why do we model human diseases?

- Experimenting on humans is generally not allowed
- To simplify a complex problem
- Ease and speed

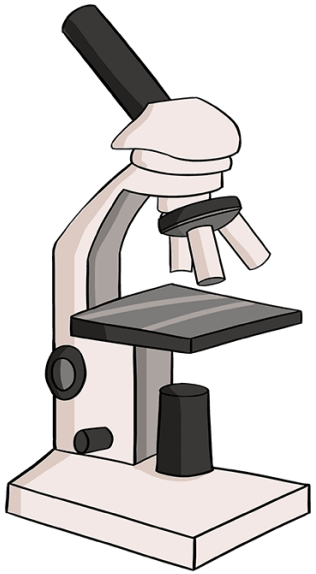
How do you make a "model"?

Genetics

Gene mutation that is known to be linked to a human disease



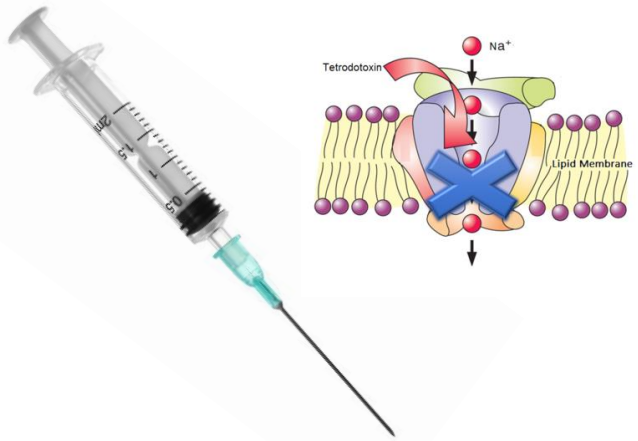
Genetically engineer organism/cells to carry mutated form of gene

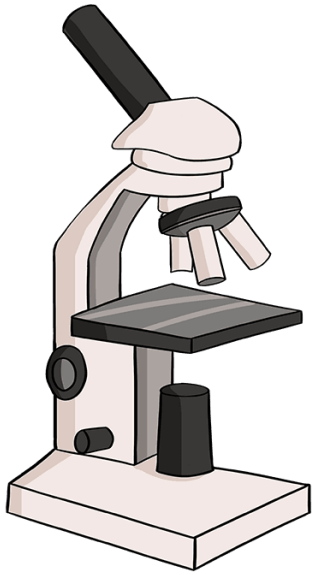


Learn more about how that mutation causes disease

How do you make a "model"?

Pharmacological





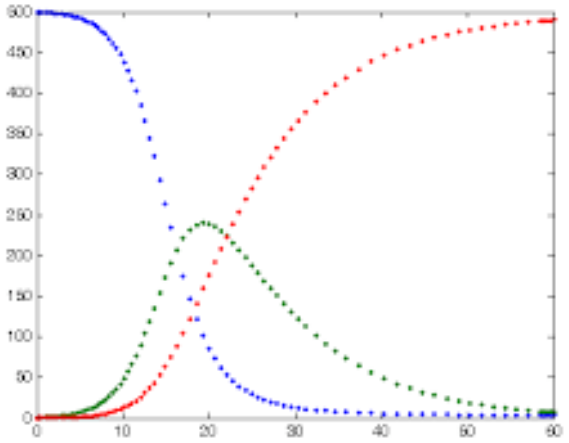
Use a drug to block/activate pathways or induce disease processes

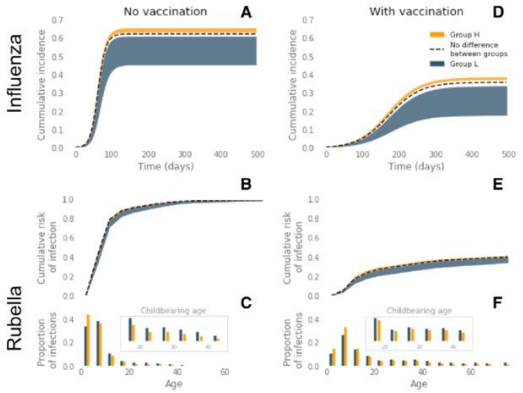
Learn more about how these pathways operate

How do you make a “model”?

Use maths!

$$v(t) = -x'(t)$$
$$x'(t) = -x(t)\left[\int_0^t A(s)\,v(t-s)\,ds + A(t)\,y_0\right]$$
$$z'(t) = \int_0^t C(s)\,v(t-s)\,ds + C(t)\,y_0$$
$$y(t) = \int_0^t B(s)\,v(t-s)\,ds + B(t)\,y_0.$$



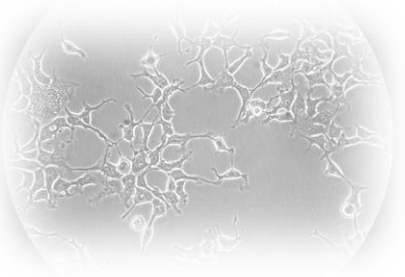


A mathematical model is an abstract description of a concrete system using mathematical concepts and language. Often used in combination with human data or data from other models.

How do you make a “model”?

Hydra

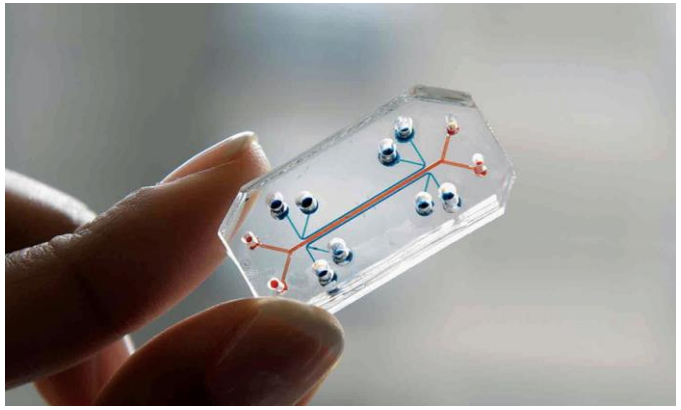
Wax moth



Cells in a dish

Rat

Sea urchin



Organ-on-a-chip

Zebrafish

What to consider when choosing a model

Is your model of choice appropriate for what you want to study?

- Does it have your gene of interest?
- Does it have the cell types you want to study?
- Are the processes you want to investigate the same as in humans?

e.g. fruit flies do not have the same immune system as humans, so looking at certain aspects of infectious diseases cannot be done in flies

There is no perfect model

- Scientists have to be aware of the limitations of their model.
- Complementary approaches are best.
- Scientific discoveries are built on years of research using different models.

Let's compare!

Fruit fly

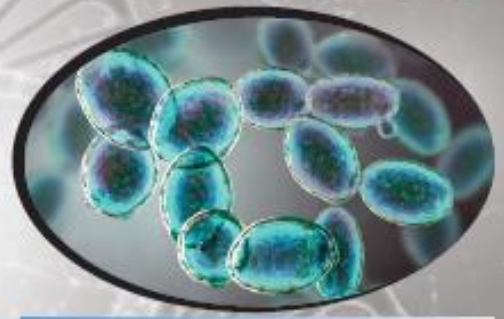
Drosophila melanogaster

Size	3 mm
Speed	7
Popularity	2323
Genome Size	180 million
Replacement Potential	3

75 % of human disease-causing genes have an equivalent in the fly. They are cheap to maintain and breed quickly, making them a useful model for studying human development and disease.

Yeast

Saccharomyces cerevisiae



Size	3 µm
Speed	10
Popularity	4009
Genome Size	12 million
Replacement Potential	5

Saccharomyces cerevisiae is a fungus that has been widely used in brewing and bread making for centuries. More recently it has been used as a model of cell growth, division, and even ageing.

Mouse

Mus musculus

Size	200 mm
Speed	2
Popularity	86,142
Genome Size	2.7 billion
Replacement Potential	1

Mice are the most commonly used animal model, accounting for over 50% of animal use in the UK. As mammals, they can mimic aspects of many human diseases.

What does the size of a model mean for a scientist?

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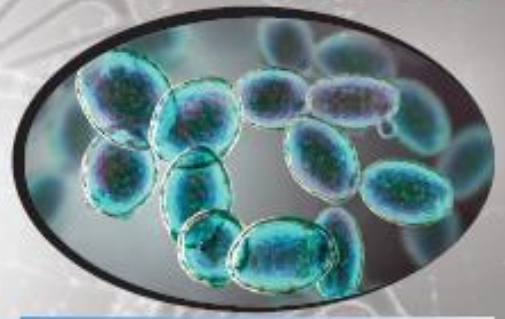

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What are the advantages/ disadvantages associated with how big the system is?

What does the "speed" of a model mean for a scientist?

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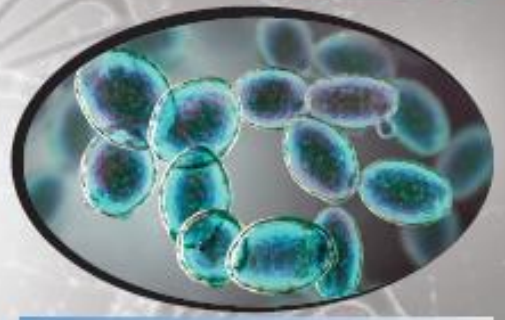

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In this case, we mean how fast scientists can carry out experiments, rather than how fast they are running...!

What does the "popularity" of a model mean for a scientist?

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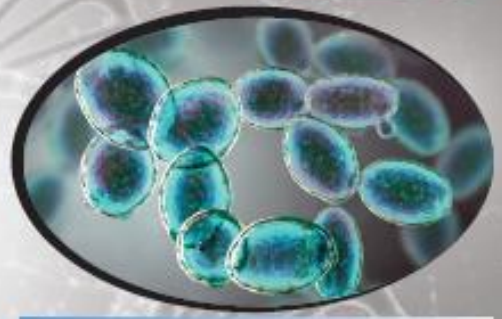

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How many articles that are published in scientific journals (in this case, in 2019).

Does popular mean better?

What does the genome size of a model mean for a scientist?

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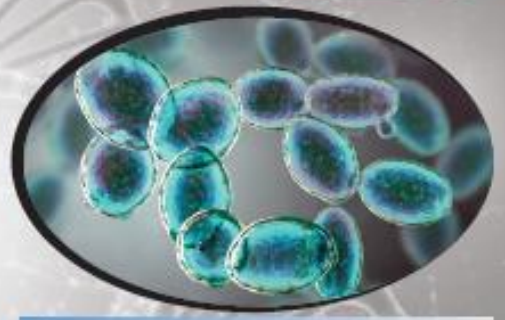

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Does a bigger genome = more complex organism?

Are there other aspects of the genetic makeup of the organism that are more important?

What does the "replacement potential" of a model mean for a scientist?

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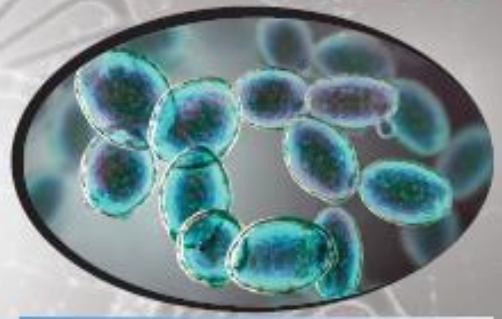

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Many scientists who use animals in their research are committed to finding alternatives.

Choose your models...

In your groups, you have a pack of Trump cards. Divide them between you and think about which models you think are the best for each research aim, and why. You have **15 minutes** to choose **three** for each.

1. You want to investigate the role of exercise on the risk of developing motor neuron disease.
2. You are interested in the role of a particular protein in cell division in cancer. This protein is similar between all species.
3. You want to understand more about how different brain cells communicate to influence addiction behaviour.

Summary

Using biological models can help us to understand the processes involved in human diseases.

Scientists use complementary approaches to solve biological problems.

Different models have advantages and disadvantages.

Understanding the limitations of the model you choose is important.