

Introduction to modelling and an application in biology

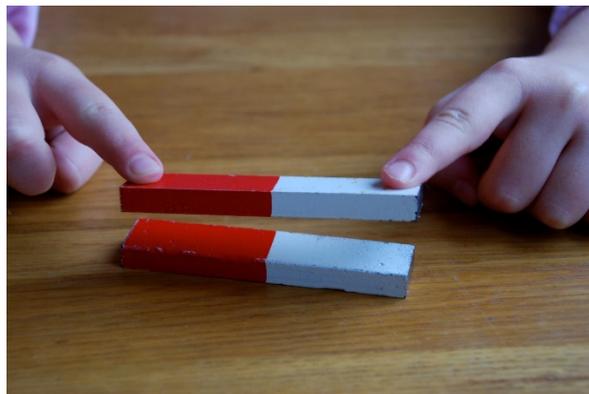
A model is a simplified representation of an object we want to study (in science, we often call this object the “system”), that captures its defining characteristics. This may seem a very abstract idea at first glance, but we can find examples of this concept in our daily lives. For instance, “model cars” look exactly like the real ones – they capture their most defining characteristics – but they are also simplified, because they are smaller and don’t have all the inner workings of real cars.



*A real Mini Cooper and a model of it.
Photo credits: smkybear (Flickr), emrank (Flickr)*

In science, what we call models are sets of hypotheses about how a system works. They can be formulated in equations, using simple diagrams, or even in plain English.

In biology, we are most interested in models describing interactions. First, let us consider magnetic attraction as an example. It is well known and easy to observe that two magnets will attract each other if they face a given way, but repel each other if they face the other way.

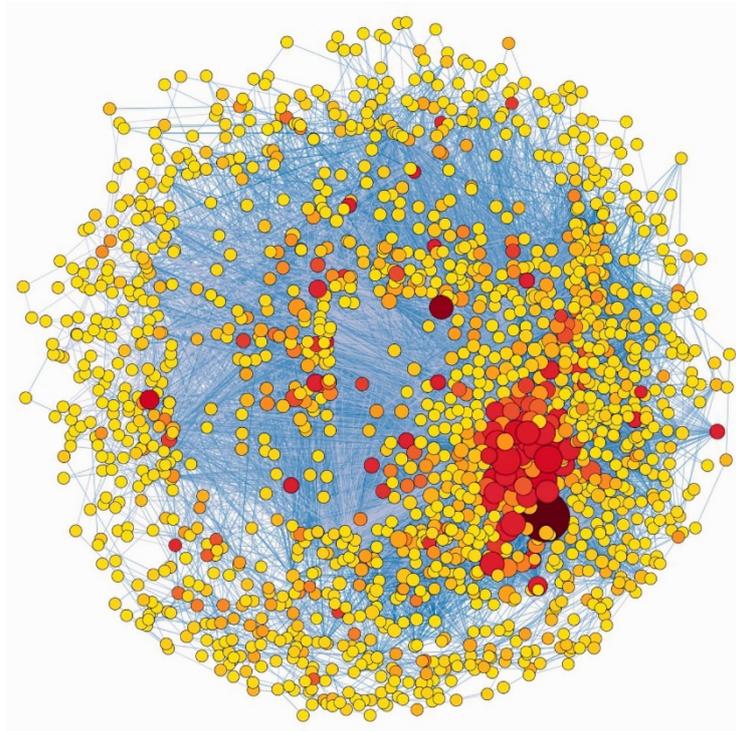


Two magnets repelling each other.

In the case of repulsion, a simple model would be that each magnet exerts a force on the other, pushing it away. This is an interaction between two separate objects.

Let us now consider a biological system as an example. Biological systems are the products of self-enforcing developmental programs, coded in genes. In real biological systems, genes are many and form complex networks of interactions.

The following network of genes is actually already very simplified (only a fraction of genes are represented).

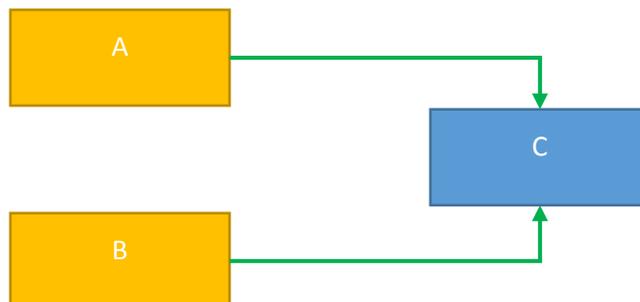


Graph of the interactions between genes of Arabidopsis thaliana (most commonly used species in plant biology). Circles represent genes and blue lines represent interactions between genes. The size and the intensity of a circle represent the number of interactions a gene has and the number of interaction pathways that pass through the gene respectively.

Source: Aluru, Maneesha, Jaroslaw Zola, Dan Nettleton, and Srinivas Aluru. "Reverse Engineering and Analysis of Large Genome-Scale Gene Networks." Nucleic Acids Research 41, no. 1 (January 1, 2013): e24–e24. doi:10.1093/nar/gks904.

To make things manageable, we will only consider a very simple model of 3 genes: A, B and C.

- Gene A activates gene C
- Gene B activates gene C



Representation of a simple 3-gene model.

What we try to capture here is the behaviour of C: when is it activated, and when is it not?

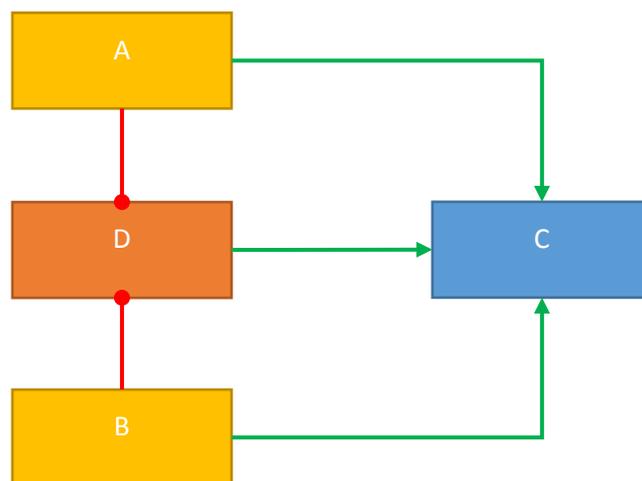
This is a simple example, but there is actually more than meets the eyes. The issue here is that the description is ambiguous. One interpretation of this model is that either A or B can activate C. However it is not the only one: A and B might both be required to activate C. This kind of ambiguities often arise in biology – not out of neglect, but simply because it is impossible to study all possible interactions in a complex network. So to address this issue, we can resort to mathematical modelling.

Boolean models can be used to specify in a formal, unambiguous language how multiple signals interact and what their combined outcome is. They represent each gene by a value (0 or 1, off or on), and each interaction by a logical rule, such as “C is on if both A and B are on”.

Mathematical models can therefore be seen as a way to store information without loss.

They can however also be used to detect gaps in our knowledge. Let us assume our current belief is “C is on if both A and B are on”, because experiments have shown that turning either A or B off results in C being turned off as well.

Now, new results become available, showing that if both A or B are off at the same time, C is on. This may sound unlikely, but it is actually possible, because many genes were omitted in this model. If we add another gene D that also activates C but is only on when both A and B are off, we can explain all observations.



A possible expansion of the model that could explain the new observations.

Thus, mathematical models are also a way to explore possibilities and make predictions of system behaviour, without having to check everything by laboratory experimentation.

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