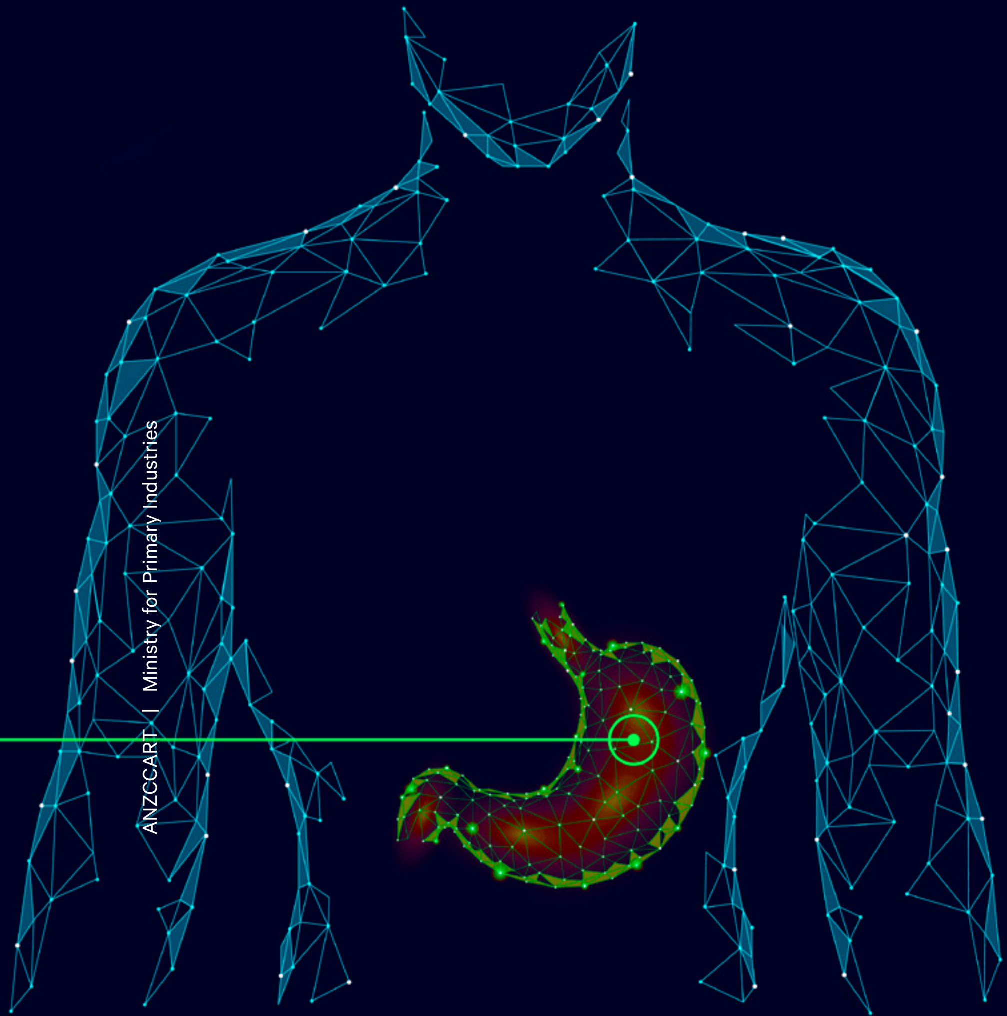
Reducing the numbers of animals in scientific research

Mathematical models



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Mathematical models of the gut

Scientists are busy developing some really exciting high-tech methods to **replace** the use of many animals in scientific research, like organs-on-a-chip, and mathematical modelling. But where human safety regulations mandate animal research, the principles of **reduction** and **refinement** are crucial.

replacement: *where possible, replacing animal use with alternative techniques*

reduction: *using the least number of animals possible while still getting useful, reliable data*

refinement: *minimising potential suffering and improving animal welfare*

What problem are scientists trying to solve?

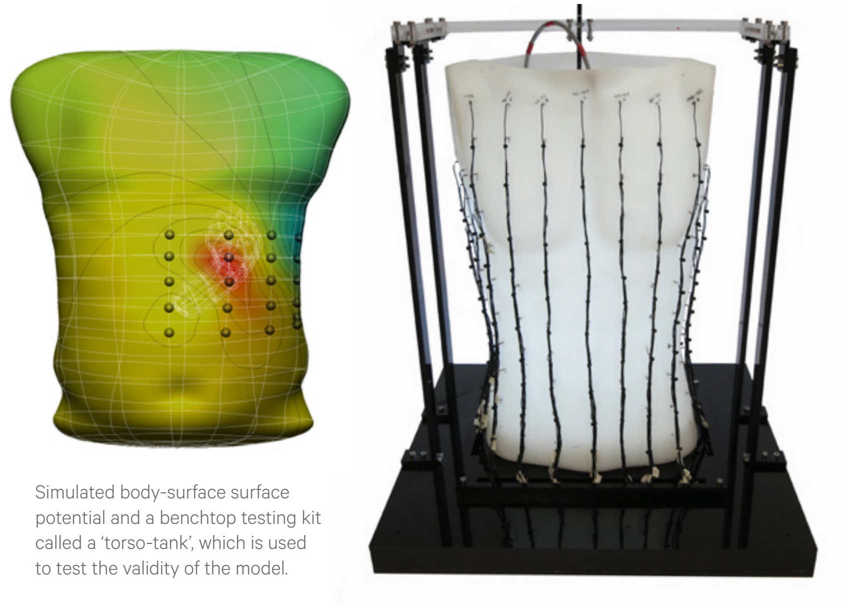
The gut is a muscle which works hard to break down the food we eat so we can extract the nutrients we need to stay healthy and recover from illnesses. Just like the heart, when the gut muscle contracts, it generates an electrical pulse, called a slow wave, which coordinates the movement of the gut. Studying gut slow waves provides a means to understand digestive health and identify disorders quicker and more accurately.

Animal experiments are a critical step in gut research. They provide valuable data that is necessary to understand how the gut works and how diseases progress. Animal studies are also a required to provide reassurance that medical devices and instruments are safe before they are applied to human subjects. Conventionally a certain number of animal subjects are needed for this, but what if there was another way?

The solution

Mathematical modelling

Mathematical modelling is a way of describing a system using mathematical concepts and equations. These models can then be tested using a variety of settings to examine the relationships between different factors that make up the system. The findings can then be used to compliment experimental data from animals. This combination of using mathematical modelling and animal data can **reduce** the number of animals needed to understand how a particular system works. Once the mathematical models have been shown to be accurate, they can **refine** how experiments are carried out in animals, or even **replace** the need for animals altogether.

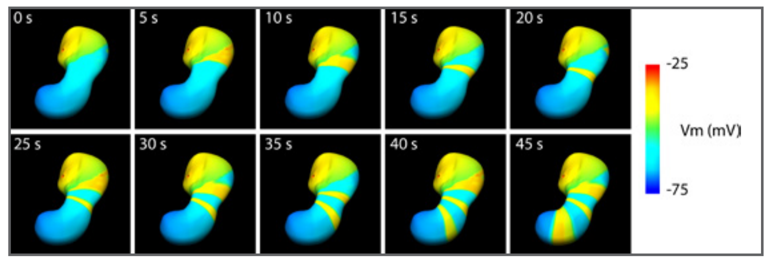


Simulated body-surface surface potential and a benchtop testing kit called a 'torso-tank', which is used to test the validity of the model.

How is it done?

In most large animal species, the stomach produces slow rhythmic waves at approximately 3 – 5 cycles per minute. Using differential equations, scientists can mathematically model these slow waves. Scientists have used these models to investigate how isolated gut muscle cells respond to electrical stimulation, which has been proposed as a potential way to help the gut recover after it has suffered a disease. Combining their mathematical models with experimental data from animals, allowed the scientists to reduce the number of animals in their study from 24 to seven.

A mathematical model of the human stomach generated from medical images.



Simulated sequence of electrical activation in the human stomach. Yellow colour represents active gastric tissues.

Advantages

- Mathematical modelling reduces the number of animals used in research and teaching.
- It allows protocols to be refined before they are applied in animal experiments.
- It potentially replaces the need for animal experiments under very specific conditions.
- Experimental data can be integrated into the model and extended beyond what the data on their own are capable of showing.

Disadvantages

- Mathematical models require validation so cannot replace animal studies until after validation.
- The validity of results are highly dependent on the sophistication of the model and how the model is applied.
- Specific software and high-performance computing hardware are often required for large-scale simulations.

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