# Crossing scientific boundaries to understand the rejection of drugs

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A physicist from The University of Nottingham and a mathematical modeller from The University of Southampton are joining forces in the hope of answering a biological mystery — how do our bodies reject some of the drugs that are sent to cure us?

The £92,300 study is funded by the Medical Research Council through its 'Discipline Hopping' Awards scheme which aims to provoke new collaborations between the physical and life sciences.

For the next 12 months Dr Cyril Rauch, physicist and lecturer in the School of Veterinary Medicine and Science at Nottingham will be working with Dr Giles Richardson, from the School of Mathematical Sciences in Southampton to find out why and how the molecules that oppose drug entry into cells work.

Dr Rauch said: "I am a physicist who is very interested in complex systems such as biology. We will be working at the interface of science — mathematics, physics and biology. Drugs have got to have a molecule in the body to target. But a drug has to cross all the body tissues prior to reaching its target and this is incredibly tricky and very difficult from the drug standpoint. In particular, cells have specific proteins, namely membrane transporters, that impair the transverse movement of drugs by constantly extruding them — these are their natural defence mechanism to avoid toxicity. We have previously suggested and reported that the membrane of cells is central and that basic physics may shed light on this very complex transport of drugs to their target. In due course we aim to

control drugs' oral bioavailability and multi drug resistance."

Dr Richardson, whose mathematical expertise is in modelling biological and electrochemical phenomena said: "When I first heard about it I was intrigued by multidrug resistance and, in particular, by the fact that, despite there being a number of well attested properties displayed by multidrug resistant cells, there is still no consensus on the mechanisms for this strange phenomenon. Furthermore I felt that the modelling techniques that I use could play an important role in testing out hypothetical mechanisms".

Multidrug resistance is a major problem in the treatment of a variety of diseases including malaria, cancer and certain bacterial infections.

Transporters on the cell's protective shield — its biomembrane — repel the drugs and are part of the mechanism that decides which particles are friend or foe. These cells will fight against drugs by putting in place drug entry systems. What Dr Rauch and Dr Richardson want to know is how and why a drug should come into contact with a transporter and be expelled and what leads to that rejection.

Research has already given us some clues as to why this happens but more work needs to be done. Together these two scientists, from very different academic backgrounds, will build on the work that has already been carried out. They want to model theoretically, using physics and mathematics, the process of drug resistance and compare these results with other experimental data.

They want to try and discover what holds the drug long enough in the membrane, which is just five nanometres thick, for it to defuse to the transporter. If they can impair diffusion of the drug to the transporter they should be able to help the drug pass safely through the membrane to the nucleus. The two scientists believe that rational mathematical

modelling has an important role in explaining this phenomenon and will eventually lead to the development of new treatment regimes.

Understanding the physical biology of therapeutics crossing cells may well lead to the generation of new therapeutic strategies that will also target cellular compounds that drive and put in place the physical biology of cells.

Source: University of Nottingham