

# Medic that switched tracks

Bengt Persson, professor at the Department of Cell and Molecular Biology, has always had a keen interest in data. But it was only after completing his medical training that he chose to make it a career interest, too. As a bioinformatician, he develops techniques and computer programs to produce new tools for managing and analysing the huge volumes of data generated by modern biomedical research.

“It is a very powerful way for us to investigate questions of interest to medicine. Furthermore, having access to the clinic as well as lab methodologies offers us incredible opportunities – it is fabulous,” says Bengt Persson.

They are trying to understand the underlying causes of various diseases by mapping out the different molecular mechanisms. A lot of this involves protein chemistry and determining the relationship between protein structure and function. Investigating the effects of various genetic changes (mutations) is one such approach.

“We might be able to predict how genetic variation affects and causes differences at the individual level. Examples here include the risk of susceptibility to particular diseases, and individual sensitivity to different drugs. These are of great medical interest.”

If the effects of different mutations are predictable, it could enable us diagnose severe mutations much earlier, sometimes even before they have had time to cause symptoms. This is particularly important for diseases where early diagnosis is vitally important. They hope to use bioinformatic methods to determine whether a mutation is harmful or benign. In a collaborative project with Karolinska Institutet, funded by AstraZeneca, they are looking at gene expression in two types of heart failure: one with reduced and one with maintained pumping ability in the left ventricle. They collect samples from patients and investigate gene expression, protein levels, metabolites and physiological properties.

“We hope to advance our understanding of how the body’s proteins function, and to use that new information to come up with ideas for new drugs. And with more accurate methods that are significantly faster than those available today,” says Bengt Persson.

They use modelling software in the computer to work out the different protein structures and predict their functions. The computer can predict how various DNA modifications might



lead to different properties, such as substrate specificity, DNA binding or impacts on protein interactions. Bengt Persson mentions that ten years ago, it could take ten weeks to produce a model. It now takes less than a day, which opens up completely new possibilities.

The research team is also developing systems for grouping protein families, comparable with the systematic work that Linnaeus did for plant life. The proteins are classified using the structural properties that provide information about their functions. One family may contain more than 100,000 proteins. And then there are subgroups and subfamilies. The team is studying two large super-families of proteins, SDR and MDR (short- and medium-chain dehydrogenase/reductase). These are centrally important to metabolism in all organisms.

“We are trying to automate this classification, but it is by no means straightforward. Some families are extremely complicated. To give an indication, one family had 20 members in 1991. Today, it has a quarter of a million, so it is all on a huge scale, to say the least,” says Bengt Persson.

They have not yet reached their goal, but are well on their way. If we can get this to work, the methodology will be applicable generally to all protein families. This will facilitate the large-scale analyses of various organisms being undertaken worldwide, says Bengt Persson. He arrived at Uppsala University and SciLifeLab in 2013, after having worked as professor in Linköping for over ten years. Today, he is also director of Sweden’s bioinformatics infrastructure, BILS/NBIS.

“The more data there is available, the more there is to discover. We are in a very exciting era in medical research, so I am glad I made this choice,” says Bengt Persson.