Combating viruses is an evolutionary problem. RNA- and retro-viruses in particular have very high evolutionary rates due to both the error-prone nature of their polymerases and strong selection pressure from the immune system. Viral proteins must therefore escape the immune response while also remaining folded and functional.

We have developed a number of computational tools that allow us to study the functional effects of amino-acid alterations in the context of protein structure. I will present the results of applying these tools to studying the evolutionary trajectories of HIV-1 and ebolavirus. For HIV-1 we find mutations that confer resistance to anti-retroviral drugs spread rapidly through the population despite their destabilising effect on protein structure. We also find that resistance-mutations are frequently preceded by replacements that stabilise the protein structure. By contrast, ebolavirus shows few signs of adaptation to humans. These observations inform the likelihood of future outbreaks and the most appropriate way of combatting them. In addition, the methods we use are generalizable to the study of sequence variation in a range of other systems.