Our bodies are under constant attack from potentially pathogenic bacteria and viruses in our surroundings. In order to cause disease, such microorganisms must enter the human host, bind to and invade specific cell types, and grow and replicate. Some pathogens make us sick by hijacking the host cellular machinery. For example, dengue virus is responsible for infecting hundreds of millions worldwide per year, and in the worst cases causes dengue hemorrhagic fever and shock syndrome. In order to fill existing gaps in our molecular understanding of the viral life cycle, we have been integrating structural, biophysical, and genomic experiments with multiscale modelling, towards the “virtual dengue virus”, and recently identified large-scale viral particle dynamics associated with infectivity and resistance to antibodies and vaccines. On the other hand, many pathogens release toxins that can make us ill through interactions with our immune system. For example, some innate immune receptors are the first line for detecting toxins derived from bacterial membranes, but excessive receptor activation can lead to sepsis, a condition that kills millions of people each year. We have developed computational models to trace in molecular detail the interplay between innate immune pathways and bacterial membranes, and leveraged these models to establish previously undisclosed modes of action of both endogenous anti-inflammatory peptides, and a novel class of antibiotics. Coming full circle, we have recently identified an interaction between such bacterial toxins and SARS-CoV-2, which may help to explain the severe COVID19-induced hyper-inflammatory disease states in patients with some comorbidities. Collectively, our work is unravelling the key determinants governing host-pathogen interactions, and contributing to the search for novel therapeutics to tackle antimicrobial resistance.