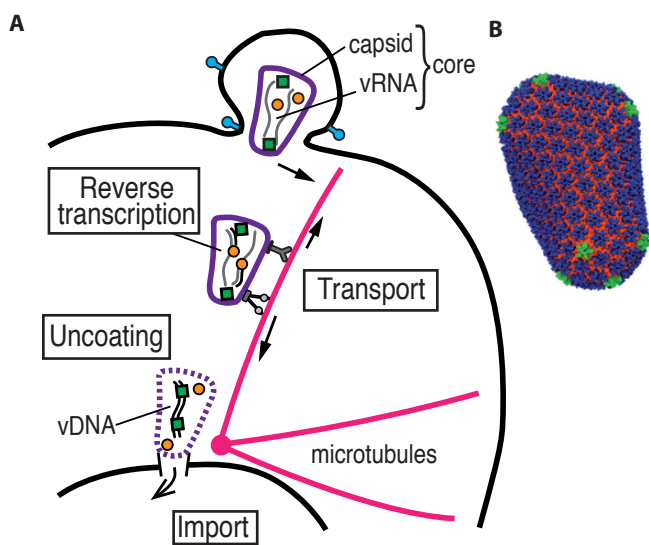


# Structural virology and Molecular machines

...visualising the molecular host-virus arms race

## How does HIV subvert the innate immune system to establish infection?

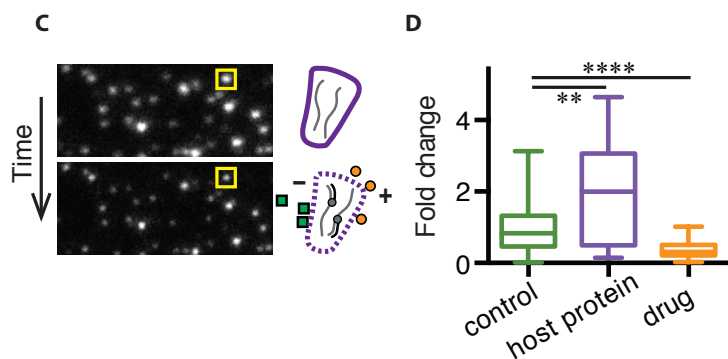
The HIV capsid protects the viral genome on its journey to the nucleus. We aim to decipher how HIV hijacks host proteins to control movement and opening of the capsid. We use a combination of structural biology, fluorescence microscopy, biochemistry and cell biology/virology.



**A.** After cell entry, HIV hijacks molecular motors to move on microtubules and enters the nucleus via the nuclear pore complex. **B.** Structure of the viral capsid.

## Observing real-time viral dynamics - one molecule at a time

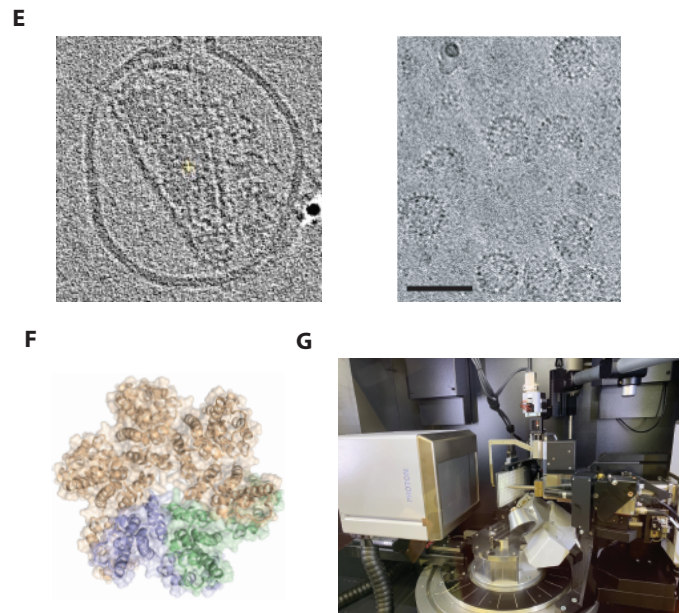
We develop new fluorescence imaging methods to track molecular processes such as viral movements on microtubules, capsid disassembly and reverse transcription at the level of individual viruses with single-molecule resolution. Our approach includes rebuilding these molecular systems outside the cell from their components to figure out how they work. For example, we have discovered how drug molecules act to break the capsid by making it too rigid. We then test predictions from our mechanistic models using infection assays in cells.



**C.** Real time imaging of capsid disassembly. **D.** Effect of host proteins and drugs on viral uncoating.

## Resolving the structure of the virus and its components at high resolution

We use structural biology to resolve the architecture of viral capsids and how it interfaces with host cell proteins. Our approaches include: cryo-electron microscopy (including correlative light and electron microscopy) of viruses and protein crystallography of purified components. The structural methods provide atomic-level insight into the nature of the host-virus interface and are part of our suite of complementary approaches to resolve molecular mechanisms.



**E.** CryoEM images of HIV (left) and of the hepatitis B virus capsid. **F.** Crystal structure of the hexamer building block of the viral capsid. **G.** X-ray diffractometer at UNSW.

## Our team

We are an interdisciplinary team of biophysicists, biochemists, cell biologists and virologists working together to decipher viral and immunological processes at the molecular level. We are looking for interns, Honours students and PhD students who like to think outside the box. Projects include: HIV, hepatitis B virus and SARS CoV2.

