Girton College Ceremony for the Commemoration of Benefactors 17 October 2020

A reflection by Dr John W Wills

Hertha Ayrton Research Fellow in Biological Sciences

Ladies and Gentleman, Fellows, Mistress: I'd like to tell you how much it means to be a Research Fellow at Girton — appointed by the Yarrow board, named in honour of Alfred Yarrow's legacy. To do this, it is probably customary for me to describe some of the research that I've been able to do since coming to Cambridge. But, to be successful in explaining what it means, it is necessary to go further. To try to explain why there is such tremendous joy here intertwined with the characters of the Cambridge landscape and the simple pleasure of finding things out.

From an early age I have been interested in nature, photography and science. At some point, this coalesced into a fascination with microscopy as a means to understand biological things.

We're all familiar with the idea of a picture's worth a thousand words – but the issue is that the pictures from modern microscopes are simply vast. So much so, they wouldn't fit in a way we could step back and make sense of, even if they were printed on bill-boards by the roadsides. And, even if we could take in the view from a distance, we would miss all of the intricate detail. What's required then is simultaneously to be the ant crawling over the local surface, and the satellite watching from overhead. To that end, computers with their uncanny ability to work hard without sleep for days on end are increasingly required to make sense of it all.

At the current time, the 'big picture' I'm trying to make sense of involves the biology of our intestine, and the fiendish task this system is entrusted with in terms of recognising friend from foe.

You see, with every mouthful of food we eat, a host of microbes come along for the ride. Some are harmless enough, some even content to seek out a symbiotic lifestyle – setting up life inside our gut as home. Others however are more nefarious – keen to break into our bodies and exploit our biology to their own ends. Against this backdrop, we trust our gut to take up the nutrients we need for life, whilst

coordinating an immune response against anything harmful. Welcome then, to a surveillance state, or at least to our states of constant immunosurveillance.

The 'big picture' I try to capture, interpret and understand involves one of the systems that is a part of this process. Fittingly for Yarrow, it involves a fleet of cargo ships. It turns out that, right now, our body is actively secreting small mineral particles into the lumen of our intestine. Here, these clump together, forming porous particles that entrap fragments of food and bacteria that are passing through. These 'particle ships' and their entrapped cargo then sail cross the gut wall, and their cargo-content is released to local immune cells. This is an education process that tries to instruct our immune systems to avoid friendly-fire (such as food allergies) whilst also priming the whole body for defence should anything more harmful be detected.

The hope is that one day, when we really understand how this system works, we may be able to engineer our own cargo for transport. This would then open up a new route for treatments for inflammatory bowel diseases, or even a means to deliver vaccines orally.

Obtaining images of this system first requires several days of precision toil in the laboratory. If nothing goes wrong, the next stage is to rattle off by bike, along the cobbles of Cambridge, with the box of prepared slides in the backpack. Anticipation builds in the hope of finding something new, spurred on by the landscape and the people who have walked here before and changed things.

Most of the time though, the experiment fails, and it's back to square one and starting over. Just occasionally however, the view is breath-taking. Just sometimes, there's something new to be seen which feels *important* – even if it may be many more years or someone else who finds what it all means.

Outcome as it may, it is usually now the small hours. Exhausted, it is time to zig-zag the revellers in the city-center, puff up Castle Hill, then off along the flat towards our college home.

Simply put, our benefactors' gifts matter because they transcend lifetimes to enable people. Coming to Girton has changed my life – both in and out of research – and I remain more grateful that I can say in words.