

# **Non-equilibrium physics of antigen recognition**

ShenShen Wang

## **1. Abstract**

Biological systems learn by accumulating incremental changes to better suit future environments. Our immune system does so through a rapid evolutionary process inside the host that improves antigen recognition on the fly. However, this Darwinian-like process appears surprisingly ineffective – why and how so remains a key puzzle. Curiously, rather than relying on equilibrium binding, immune cells physically acquire antigens from other cells using active forces. We build a mathematical framework to explore whether, and when, non-equilibrium antigen recognition confers an adaptive benefit. By assessing the macroscopic impact of microscopic dynamics, we show how non-equilibrium recognition limits response potency to current targets, yet enables plasticity against future variants. This multi-faceted role of physical forces may balance the depth-breadth tradeoffs within a finite repertoire.