qbSS 2018 Student Presentation – ABSTRACT

Cell fate decisions in innate immunity

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Using a rule-based stochastic model of the NF-κB signalling network alone and in combination with IRF3 and STAT1 signalling, we investigated how the innate immune system processes pathogen-derived signals into cell fate decisions. (1) Having explicitly modelled the interactions of NF-κB with karyopherins (nuclear transport proteins), we found that in response to TNF they enable a near-minimal resetting time of the system, supporting its digitisation. (2) We demonstrated that the amount of information between experimental TNF concentration and level of nuclear NF-κB, estimated at 1 bit is only weakly affected by increasing TNFR-associated extrinsic noise, which also supports digitisation of the response, and frames the NF-κB network as a decision-making module. (3) In the more comprehensive model, we showed that positive feedback and positive feedforward by auto- and paracrine IFNβ-STAT1 signalling mediate integration of signals over longer time courses, thus distinguishing between viral and bacterial infection. The nonlinear transmission elements convert pathogen-associated signals into predefined responses, which, when combined with paracrine signal propagation, result in shorter cell fate decision phase and coordination of responses across the cell population.