

# **Spatially distributed network between EGFR and phosphatases optimizes growth factor sensing at criticality**

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The proto-oncogenic epidermal growth factor receptor (EGFR) is a tyrosine kinase whose sensitivity to growth factors and signal duration determines cellular behavior. We resolve how the phosphorylation response of EGFR to epidermal growth factor originates from dynamically established recursive interactions with protein tyrosine phosphatases (PTPs). Using advanced single cell microscopy techniques and dynamical systems theory we revealed how vesicular recycling of EGFR unifies the interactions with PTPs that are localized on distinct membranes to generate a spatially distributed network architecture that dictates how cells sense and respond to time varying growth factor signals. These signal processing characteristics result from the intrinsic organization of the network close to a critical region in parameter space where only a single steady state, the basal EGFR phosphorylation is stable. We therefore propose a novel concept of information processing with metastable states at criticality and demonstrate how this allows the system to translate and interpret the information about the changing environment.