

Ras signaling from nanoclusters – high fidelity nanoswitches

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Abstract: Cellular signaling networks are subject to exquisite spatial regulation. Addressing how complex networks function as control and computational systems remains a challenging task. Here we report on our in silico and in vivo analyses of mitogen-activated protein kinase signaling that Ras nanoclusters operate as sensitive switches. Each nanocluster is sensitive to low threshold input, and releases a defined phospho-ERK signaling quantum during its short lifetime. Thus it acts as an amplifying analogue-digital converter. Nanoclusters are generated in direct proportion to ligand, thus cytosolic integration of the quanta converts the digital (switch-like) output of the nanoclusters back into an analogue signal. In silico modeling showed that number and size of nanoclusters are critical for the system response. This network design allows to transmit signals with high fidelity across the membrane. In general, this design principle illustrates, how the spatial constraints of signal transduction circuits in the special environment of cellular membranes, can be used as a fundamental control mechanism.

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Abstract only