Supplementary materials

featuring article

Limits to the rate of information transmission through MAPK pathway

by

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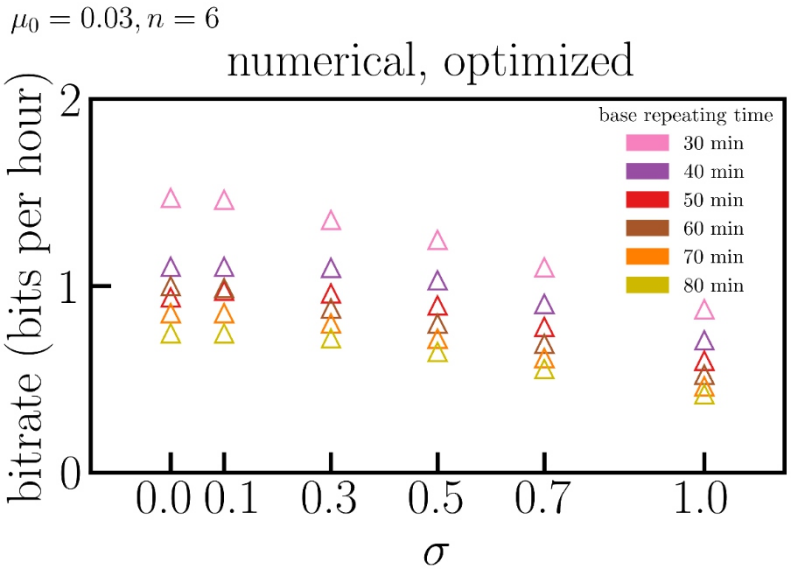
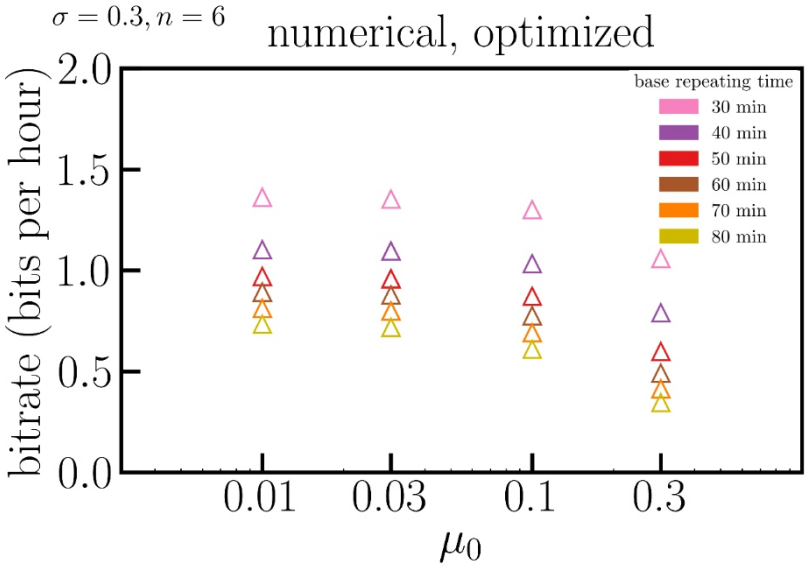


Supplementary Figure 1. Influence of cell specific noise on transmitted information. Mutual information was calculated numerically as follows: triangles – maximized, circles – assuming equal probabilities of all group representatives, squares – assuming equal probabilities of all input sequences.



Supplementary Figure 2. Influence of additive noise on transmitted information. Mutual information was calculated numerically as follows: triangles – maximized, circles – assuming equal probabilities of all group representatives, squares – assuming equal probabilities of all input sequences.

Supplementary Table 1. Parameter values for the MAPK pathway model.

Default values originate from the article by Kochańczyk *et al*. (2017), *Sci. Rep*., **7**:38244, doi:10.1038/srep38244.
The parameters of the pathway that are drawn from the lognormal distribution LogN(μ_i, σ) are written in bold green.

Parameter	**Description**
Concentrations (protein copy number per cell)	
$EGFR_{tot} = 3\times10^5$	Total number of EGFR molecules
$RAS_{tot} = 6\times10^4$	Total number of RAS molecules
$SOS_{tot} = 10^5$	Total number of SOS molecules
$RasGAP_{tot} = 6\times10^3$	Total number of RasGAP molecules
$RAF_{tot} = 5\times10^5$	Total number of RAF molecules
$MEK_{tot} = 2\times10^5$	Total number of MEK molecules
$ERK_{tot} = 3\times10^6$	Total number of ERK molecules
Rate constant for fast processes (s^{-1})	
$k_{fast} = 100$	As a simplification, three (pseudo) first-order processes considered in the model are assumed to be fast.
Rate constants for activation processes [(molecules/cell)$^{-1}$ s^{-1} except (pg/ml)$^{-1}$ s^{-1} for a_1]	
$a_1 = 5\times10^{-5}$	EGF-mediated activation of EGFR
$a_2 = 10^{-7}$	Activation of RAF by RAS-GTP
$b_1 = 10^{-5}$	Binding of EGF-activated EGFR and dephosphorylated SOS
$p_1 = 10^{-7}$	Phosphorylation of MEK's activation sites by RAF
$p_2 = 3\times10^{-6}$	Phosphorylation of ERK's activation sites by MEK
Rate constants for deactivation processes (s^{-1})	
$d_1 = d = 0.01$	Deactivation of EGFR
$d_2 = d$	Deactivation of RAF (spontaneous)
$u_{1A} = d$	Dissociation of active EGFR–SOS complex
$q_1 = d$	Dephosphorylation of MEK's activation sites
$q_2 = d$	Dephosphorylation of ERK's activation sites
Rate constants for SOS association reactions [(molecules/cell)$^{-1}$ s^{-1}] *and dissociation reactions* (s^{-1})	

$b_{2A} = 10^{-6}$	Association of SOS and RAS-GTP
$b_{2B} = 0.1 \times b_{2A}$	Association of SOS and RAS-GDP
$u_{1B} = k_{fast}$	Dissociation of inactive EGFR–SOS complex
$u_{2A} = u_{2B} = 1$	Dissociation of SOS–RAS-GTP complex and SOS–RAS-GDP complex
Rate constants associated with SOS-to-RAS positive feedback [(molecules/cell)$^{-1}$ s^{-1} except s^{-1} for k_3 and u_3]	
$k_{2A} = 10^{-4}$	SOS's nucleotide-exchange activity when RAS-GTP is bound to its REM domain
$k_{2B} = 0.1 \times k_{2A}$	SOS's nucleotide-exchange activity when RAS-GDP is bound to its REM domain
$k_{2C} = 0$	SOS's nucleotide-exchange activity when no RAS is bound to its REM domain
$b_3 = 10^{-5}$	Association of RasGAP and RAS-GTP
$k_3 = k_{fast}$	RasGAP-facilitated RAS-GTP→RAS-GDP hydrolysis
$u_3 = 0.01$	Dissociation of RasGAP from RAS-GDP after hydrolysis of GTP
Rate constants associated with ERK-mediated negative feedbacks [(molecules/cell)$^{-1}$ s^{-1}]	
$p_3 = 3\times10^{-9}$	Phosphorylation of unbound SOS by active ERK
$p_4 = p_6 = p = 6\times10^{-10}$	Phosphorylation of MEK (T292 in MEK1) and RAF by active ERK
Rate constants for (spontaneous) dephosphorylation reactions (s^{-1})	
$\boldsymbol{q_3 = q_4 = q_6 = q = 3\times10^{-4}}$	Dephosphorylation of inhibitory phosphosites in SOS, MEK (T292 in MEK1), RAF
$\boldsymbol{q_5 = k_{fast}}$	Dephosphorylation of MEK's activation sites when MEK's T292 is phosphorylated
ERK activity reporters – concentrations (protein copy number per cell)	
$EKAR3_{tot} = ERKTR_{tot} = 10^6$	Total number of EKAR3 and ERKTR molecules
ERK activity reporters – rate constants for activation reactions [(molecules/cell)$^{-1}$ s^{-1}]	
$a_{EKAR3} = 3\times10^{-9}$	EKAR3 activation rate by active ERK
$a_{ERKTR} = 10^{-9}$	ERKTR activation rate by active ERK
ERK activity reporters – rate constants for deactivation reactions (s^{-1})	
$d_{EKAR3} = 10^{-3}$	EKAR3 deactivation rate