

Table S1a

Molecule-molecule interaction	Reaction number	kf (/s/μM)	kb (/s)	Notes
	1	1.0e-4 *	1.0e-4	Constrained by <i>in vivo</i> dynamics of EGFR (Fig. 2a)
	2	2.2833	0.0029666	1,2
	3	10	0.02	3,4
	4	4	0.001	3,5,6
	5	0.5	0.2	On the basis of ⁷ , further constrained by <i>in vivo</i> dynamics of EGFR (Fig. 2a)
	6	0.05 *		On the basis of ⁷ , further constrained by <i>in vivo</i> dynamics of EGFR (Fig. 2a)
	7	0.001 *		Constrained by <i>in vivo</i> dynamics of EGFR (Fig. 2a)
	8	10	0.2	3,4
	9	1 *		On the basis of ⁸ , further constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)
	10	1	0.2	On the basis of ⁹ , further constrained by EGF-dependent Rap1 activation (Fig. 2d)
	11	1 *		On the basis of ⁹ , further constrained by EGF-dependent Rap1 activation (Fig. 2d)
	* denotes /s.			

Enzymatic reaction	Reaction number	Km (μM)	Vmax (/s)	Notes
	1	0.1	0.2	10

Initial concentration	Molecule	CoInit (μM)		Notes
	EGFR	0.3		3
	pro_EGFR	0.3	constant	3,11
	Shc	1		3
	c-Cbl	0.5		On the basis of ¹² , further constrained by <i>in vivo</i> dynamics of EGFR (Fig. 2a)
	FRS2	1		13
	Dok	0.3		Constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)

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Table S1b

Molecule-molecule interaction	Reaction number	kf (/s/μM)	kb (/s)	Notes
	1	8.333e-4 *	2.7778e-4	¹
	2	6.2	6.4e-5	On the basis of ² , further constrained by <i>in vivo</i> dynamics of TrkA (Fig. 2b)
	3	1 *		Constrained by <i>in vivo</i> dynamics of TrkA (Fig. 2b)
	4	6.3e-4 *		On the basis of ¹ , further constrained by <i>in vivo</i> dynamics of TrkA (Fig. 2b)
	5	4.2e-4 *		On the basis of ¹ , further constrained by <i>in vivo</i> dynamics of TrkA (Fig. 2b)
	6	10	0.2	On the basis of ³ , further constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)
	7	5	0.1	On the basis of ³ , further constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)
	8	0.1 *		On the basis of ⁴ , further constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)
	9	2 *		On the basis of ⁵ , further constrained by <i>in vivo</i> dynamics of Rap1 (Fig. 2d)
	10	0.0022 *		Constrained by <i>in vivo</i> dynamics of TrkA (Fig. 2b)
	* denotes /s.			

Enzymatic reaction	Reaction number	Km (μM)	Vmax (/s)	Notes
	1	0.1	0.02	On the basis of ⁶ , further onstrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)

Initial concentration	Molecule	CoInit (μM)		Notes
	TrkA	0.061894		⁷
	pro_TrkA	0.020631	constant	¹

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Table S1c

Molecule-molecule interaction	Reaction number	kf (/s/μM)	kb (/s)	Notes
	1	0.03	0.0168	¹
	2	10	0.2	^{1,2}
	3	0.005 *		²
	4	0.002 *		Constrained by <i>in vivo</i> dynamics of SOS (Fig. S2g, h)
	5	0.12	0.01	³
	6	0.002 *	1.0e-5	Constrained by <i>in vivo</i> dynamics of Ras (Fig. 2c)
	7	1.667e-4 *		⁴
* denotes /s.				

Enzymatic reaction	Reaction number	Km (μM)	Vmax (/s)	Notes
	1	0.02	2	⁵
	2	25.641	1	⁶
	3	1	10	⁷

Initial concentration	Molecule	CoInit (μM)	Notes
	SOS	0.1	⁶
	Grb2	1	⁶
	RasGAP	0.1	⁸
	Ras	0.1	⁶

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Table S1d

Molecule-molecule interaction	Reaction number	kf (/s/μM)	kb (/s)	Notes
	1	1	0.002	¹
	2	1	0.2	²
	3	0.005 *		Constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)
	4	1.166e-4 *		³
* denotes /s.				

Enzymatic reaction	Reaction number	Km (μM)	Vmax (/s)	Notes
	1	0.01	0.024	On the basis of ⁴ , further constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)
	2	1	2	⁵

Initial concentration	Molecule	CoInit (μM)		Notes
	C3G	0.5		Constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)
	Crk	1		Constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)
	Rap1	0.2		On the basis of ⁶ , further constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)
	Rap1GAP	0.012		On the basis of ⁶ , further constrained by <i>in vivo</i> dynamics of Rap1 activation (Fig. 2d)

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Table S1e

Molecule-molecule interaction	Reaction number	kf (/s/μM)	kb (/s)	Notes
	1	60	0.5	¹
	2	60	0.5	^{1,2}
	3	60	0.5	³
	4	0.15 *		¹
	5	10	0.075	⁴
	6	16.304	0.6	¹
* denotes /s.				

Enzymatic reaction	Reaction number	Km (μM)	Vmax (/s)	Notes
	1	0.16	0.5	¹
	2	0.16	0.2	¹
	3	0.16	0.3	¹
	4	15.657	3	¹
	5	0.02	0.06	⁵

Initial concentration	Molecule	CoInit (μM)		Notes
	c-Raf	0.5		¹
	B-Raf	0.2		¹
	MEK	0.68		¹
	ERK	0.26		¹
	PP2A	0.24		¹
	MKP3	0.018		^{1,6}

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