

Molecule	#
Osteoblast cell	1
I_d	500
$I_{f\ act}$	0
$I_{f\ act} + FAK_{act}$	0
I_{act}	0
FAK_{act}	1000
$I_{f\ act} + FAK_{act}$	1
$I_{f\ act} + FAK_{act} + RAS_d$	1
FAK_d	1
RAS_d	1000
$I_{f\ act} + FAK_{act} + RAS_d$	0
RAS_{act}	0
$RAS_{act} + RAF_d$	0
RAF_d	32
$RAS_{act} + RAF_d$	0
RAF_{act}	0
$RAF_{act} + MEK_d$	0
MEK_d	3400
$RAF_{act} + MEK_d$	0
MEK_{act}	0
$MEK_{act} + ERK_d$	0
ERK_d	2300
$MEK_{act} + ERK_d$	0
ERK_{act}	0
$ERK_{act} + RUNX2_d$	0
$ERK_{act} + OTHER$	0
$RUNX2_d$	24
$ERK_{act} + RUNX2_d$	0
$RUNX2_{act}$	0
$RUNX2_{act} + DNA$	0
OSX_{mon}	8
$RUNX2_{act} + OSX_{mon}$	0
$OSX_{mon} + DNA$	5
$RUNX2_{act} + OSX_{mon} + DNA$	0
$RUNX2_{act} + OSX_{mon} + DNA + AP1$	0
OSX_{mul}	5
$RUNX2_{act} + OSX_{mul}$	0
$OSX_{mul} + DNA$	6
$RUNX2_{act} + OSX_{mul} + DNA$	0
$AP1$	0
$RUNX2_{act} + OSX_{mon} + DNA + AP1$	0
OPN_{RNA}	0
$Rib_{av} + OPN_{RNA}$	0
$Rib_{n\ av} + OPN_{RNA}$	0
OCN_{RNA}	0
$Rib_{av} + OCN_{RNA}$	0
$Rib_{n\ av} + OCN_{RNA}$	0
ALP_{RNA}	0
$Rib_{av} + ALP_{RNA}$	0
$Rib_{n\ av} + ALP_{RNA}$	0
BSP_{RNA}	0
$Rib_{av} + BSP_{RNA}$	0
$Rib_{n\ av} + BSP_{RNA}$	0
$Rib_{n\ comp}$	299
$Rib_{n\ comp} + RNA$	0
Rib_c	301
$Rib_c + RNA$	0
$MAT + Vesc$	0

2 **Supplementary table 1: Number of molecules at t_0**

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Parameter	Symbol	Value	Unit of measure
Mechanical min. magnitude	m	100	μPa
Mechanical phase	ϕ	0	rad
Integrin activation delay	$T_{I_d \rightarrow I_f \text{ act}}$	0	s
I_d dissoc. time from I + FAK comp.	$T_{I_f \text{ act} + FAK_{act} \rightarrow I_d}$	$U[0, 80]$	s
FAK _{act} activation delay	$T_{FAK_d \rightarrow FAK_{act}}$	5	s
FAK _d dissoc. time from I + FAK comp.	$T_{I_f \text{ act} + FAK_{act} \rightarrow FAK_d}$	30	s
I_{act} + FAK dissoc. time	$T_{I_f \text{ act} + FAK_{act} + RAS_d \rightarrow I_f \text{ act} + FAK_{act}}$	7	s
RAS _{act} dissoc. time from I + FAK + RAS comp.	$T_{I_f \text{ act} + FAK_{act} + RAS_d \rightarrow RAS_{act}}$	7	s
RAS _{act} dissoc. form RAS + RAF comp.	$T_{RAS_{act} + RAF_d \rightarrow RAS_{act}}$	14	s
RAS _{act} relaxation time	$T_{RAS_{act} \rightarrow RAS_d}$	60	s
RAF _{act} dissoc. time	$T_{RAS_{act} + RAF_d \rightarrow RAF_{act}}$	14	s
RAF _{act} dissoc. time from RAF + MEK	$T_{RAF_{act} + MEK_d \rightarrow RAF_{act}}$	10	s
Relaxation of RAF _{act}	$T_{RAF_{act} \rightarrow RAF_d}$	60	s
MEK _{act} dissoc. time from RAF + MEK comp.	$T_{RAF_{act} + MEK_d \rightarrow MEK_{act}}$	10	s
MEK _{act} dissoc. time from MEK + ERK comp.	$T_{MEK_{act} + ERK_d \rightarrow MEK_{act}}$	8	s
MEK relaxation time	$T_{MEK_{act} \rightarrow MEK_d}$	88	s
ERK activation time	$T_{MEK_{act} + ERK_d \rightarrow ERK_{act}}$	8	s
ERK relaxation time	$T_{ERK_{act} \rightarrow ERK_d}$	50	s
ERK _d dissoc. time from RUNX2 + ERK comp.	$T_{ERK_{act} + RUNX2_d \rightarrow ERK_{act}}$	10	s
ERK _{act} dissoc. time from ERK _{act} + OTHER comp.	$T_{ERK_{act} + OTHER \rightarrow ERK_{act}}$	6	s
RUNX2 _{act} dissoc. time from ERK _{act} + RUNX2 _d comp.	$T_{ERK_{act} + RUNX2_d \rightarrow RUNX2_{act}}$	10	s
RUNX2 _{act} dissoc. time from RUNX2 _{act} + DNA comp.	$T_{RUNX2_{act} + DNA \rightarrow RUNX2_{act}}$	10	s
RUNX2 relaxation time	$T_{RUNX2_{act} \rightarrow RUNX2_d}$	60	s
OSX _{mon} dissoc. time from RUNX2 _{act} + OSX _{mon} comp.	$T_{RUNX2_{act} + OSX_{mon} \rightarrow OSX_{mon}}$	20	s
OSX _{mon} + DNA dissoc. time from RUNX2 _{act}	$T_{RUNX2_{act} + OSX_{mon} + DNA \rightarrow OSX_{mon} + DNA}$	30	s
OSX _{mon} + DNA dissoc. time from AP1	$T_{RUNX2_{act} + OSX_{mon} + DNA + AP1 \rightarrow OSX_{mon} + DNA}$	0	s
OSX _{mul} dissoc. time from RUNX2 _{act} + OSX _{mul} comp.	$T_{RUNX2_{act} + OSX_{mul} \rightarrow OSX_{mul}}$	40	s
OSX _{mul} + DNA dissoc. time from RUNX2 _{act}	$T_{RUNX2_{act} + OSX_{mul} + DNA \rightarrow OSX_{mul} + DNA}$	50	s
ribosome availability time from Rib _{n av} + OPN _{RNA}	$T_{Rib_{n av} + OPN_{RNA} \rightarrow Rib_{av} + OPN_{RNA}}$	20	s
OPN _{RNA} dissociation time from available ribosome	$T_{Rib_{av} + OPN_{RNA} \rightarrow OPN_{RNA}}$	75	s
ribosome availability time from Rib _{n av} + OCN _{RNA}	$T_{Rib_{n av} + OCN_{RNA} \rightarrow Rib_{av} + OCN_{RNA}}$	20	s
OCN _{RNA} dissociation time from available ribosome	$T_{Rib_{av} + OCN_{RNA} \rightarrow OCN_{RNA}}$	75	s
ribosome availability time from Rib _{n av} + ALP _{RNA}	$T_{Rib_{n av} + ALP_{RNA} \rightarrow Rib_{av} + ALP_{RNA}}$	20	s
ALP _{RNA} dissociation time from available ribosome	$T_{Rib_{av} + ALP_{RNA} \rightarrow ALP_{RNA}}$	75	s
ribosome availability time from Rib _{n av} + BSP _{RNA}	$T_{Rib_{n av} + BSP_{RNA} \rightarrow Rib_{av} + BSP_{RNA}}$	20	s
BSP _{RNA} dissociation time from available ribosome	$T_{Rib_{av} + BSP_{RNA} \rightarrow BSP_{RNA}}$	75	s
RNA dissociation time from Rib _{n comp}	$T_{Rib_{n comp} + RNA \rightarrow Rib_{n comp}}$	100	s
RNA dissociation time from complete ribosome	$T_{Rib_c + RNA \rightarrow Rib_c}$	100	s
force tag probability	F_{tag}	$P_{\{01,02\}} = \{0.9, 0.1\}$	
I_d interaction radius	R_{I_d}	50	nm
FAK _{act} interaction radius	$R_{FAK_{act}}$	50	nm
RAS _d interaction radius	R_{RAS_d}	80	nm
RAF _d interaction radius	R_{RAF_d}	70	nm
MEK _d interaction radius	R_{MEK_d}	50	nm
ERK _d interaction radius	R_{ERK_d}	30	nm
RUNX2 _d interaction radius	R_{RUNX2_d}	30	nm
OSX _{mon} interaction radius	$R_{OSX_{mon}}$	30	nm
Rib _{n comp} interaction radius	$R_{Rib_{n comp}}$	30	nm
cell radius	R_{cell}	1000	nm
nucleus radius	R_{nucl}	400	nm
protein' s average velocity	\bar{v}_p	2	nm/s
protein' s velocity variation	Δv_p	1	nm/s
protein' s direction variation	$\Delta \varphi_p = \Delta \theta_p$	$\pi/10$	rad
protein translation delay	T_p	95	s
transcription delay per mRNA	T_{RNA}	600	s
Integrins θ angle on cell membrane distribution	I_θ	$U[0, \pi]$	1/rad
Integrins ϕ angle on cell membrane distribution	I_ϕ	$U[0, 2\pi]$	1/rad

5 **Supplementary table 2: Parameters' name, symbols and values.**

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Parameter	Symbol	List of values	Unit of measure
Mechanical max. magnitude	M	{1000, 10000}	μPa
Mechanical period	P	{10000, 50000, 2000000}	s
MEK _{act} dissociation time from RAF _{act} + MEK _d comp.	$T_{RAF_{act}+MEK_d \rightarrow MEK_{act}}$	{10, 90, 300, 480, 1320}	s
MEK _{act} dissociation time from MEK _{act} + ERK _d comp.	$T_{MEK_{act}+ERK_d \rightarrow MEK_{act}}$	{8, 90, 300, 480, 1320}	s
MEK _d relaxation time	$T_{MEK_{act} \rightarrow MEK_d}$	{60, 90, 300, 480, 1320}	s
ERK _{act} activation time	$T_{MEK_{act}+ERK_d \rightarrow ERK_{act}}$	{8, 90, 300, 480, 1320}	s
ERK _d relaxation time	$T_{ERK_{act} \rightarrow ERK_d}$	{90, 300, 480, 600, 1320}	s
ERK _{act} dissociation time from ERK _{act} + RUNX2 _d comp.	$T_{ERK_{act}+RUNX2_d \rightarrow ERK_{act}}$	{10, 90, 300, 480, 1320}	s

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8 Supplementary table 3: Parameter ranges

9 Names, symbols, unit of measures and list of values simulated. Bold quantities represent the

10 baseline values. Where no baseline is present, then all possible combinations has been considered.

11 Each set of parameters has been independently repeated 10 times.