Short term synaptic plasticity and transcription regulation

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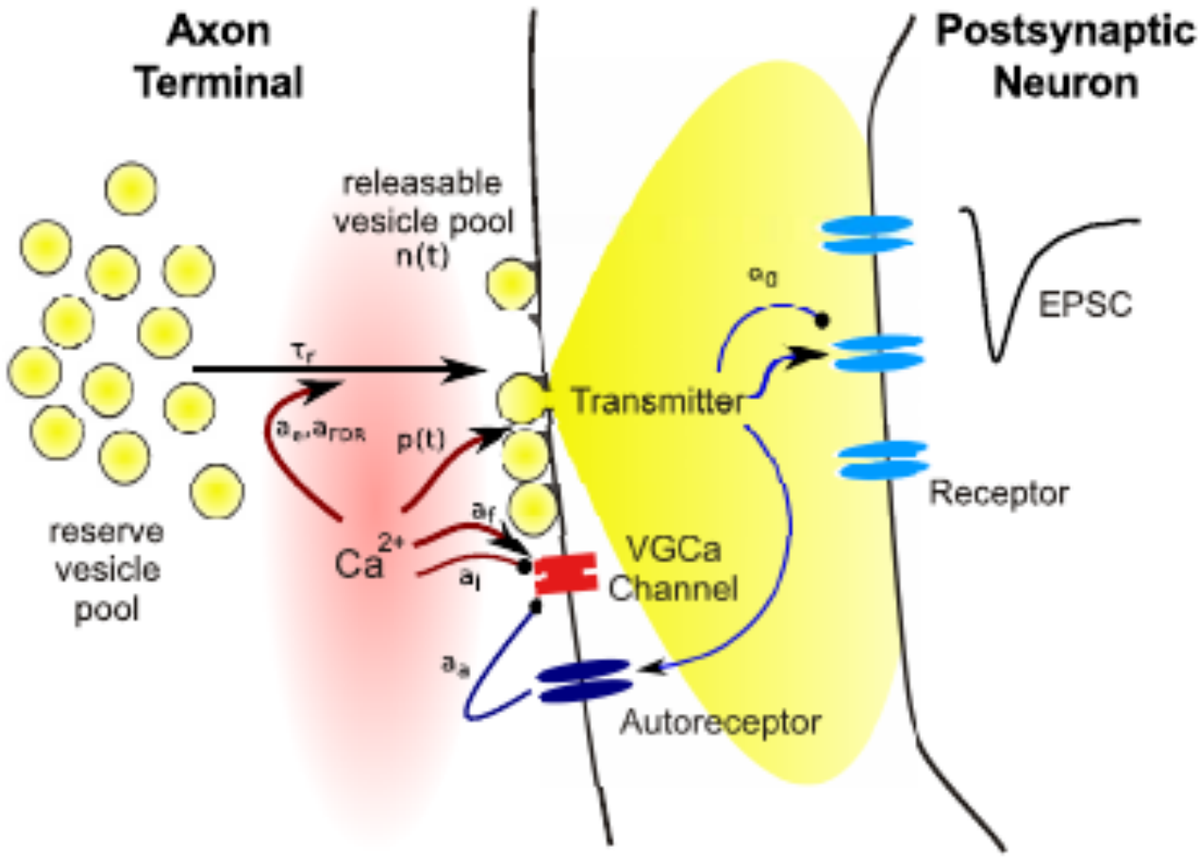


FIGURE 1 | Schematic illustration of the main steps involved in synaptic transmission, and of variables subject to use-dependent modification. Symbols refer to quantities used in the model equations in this review.

Let represent an average $c_a = [Ca]_i$ in axonal terminals forming a synaptic contact. Let p and x represent the probability of release and the density of readily releasable vesicles in the terminal. A simple model for the dynamics of presynaptic release is then

$$\partial_t c_a = \frac{c_{a\infty} - c_a}{\tau_c} - kI_N(v_a) \quad (1)$$

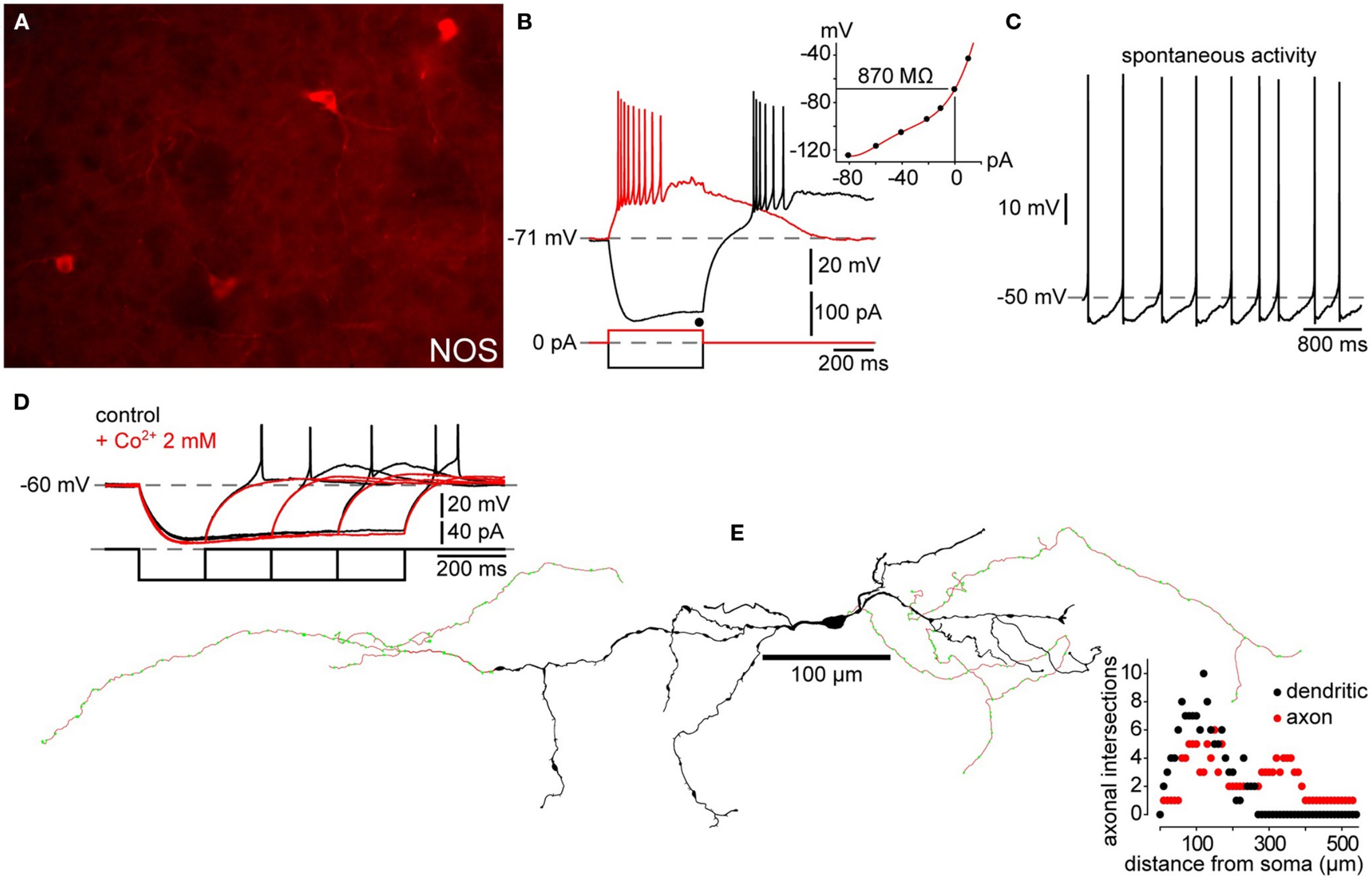
$$p_\infty(c) = \frac{c^l}{c^l + {c_m}^l} \quad (2)$$

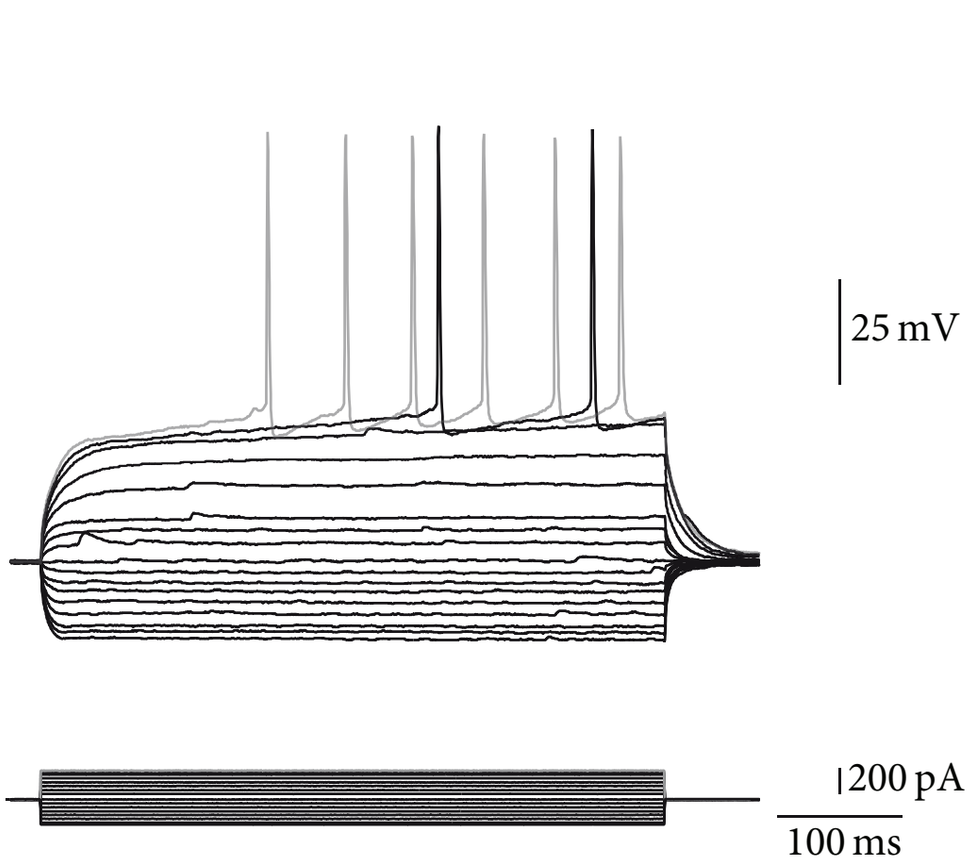
$$\partial_t p = \frac{p_\infty(c) - p}{\tau_p} \quad (3)$$

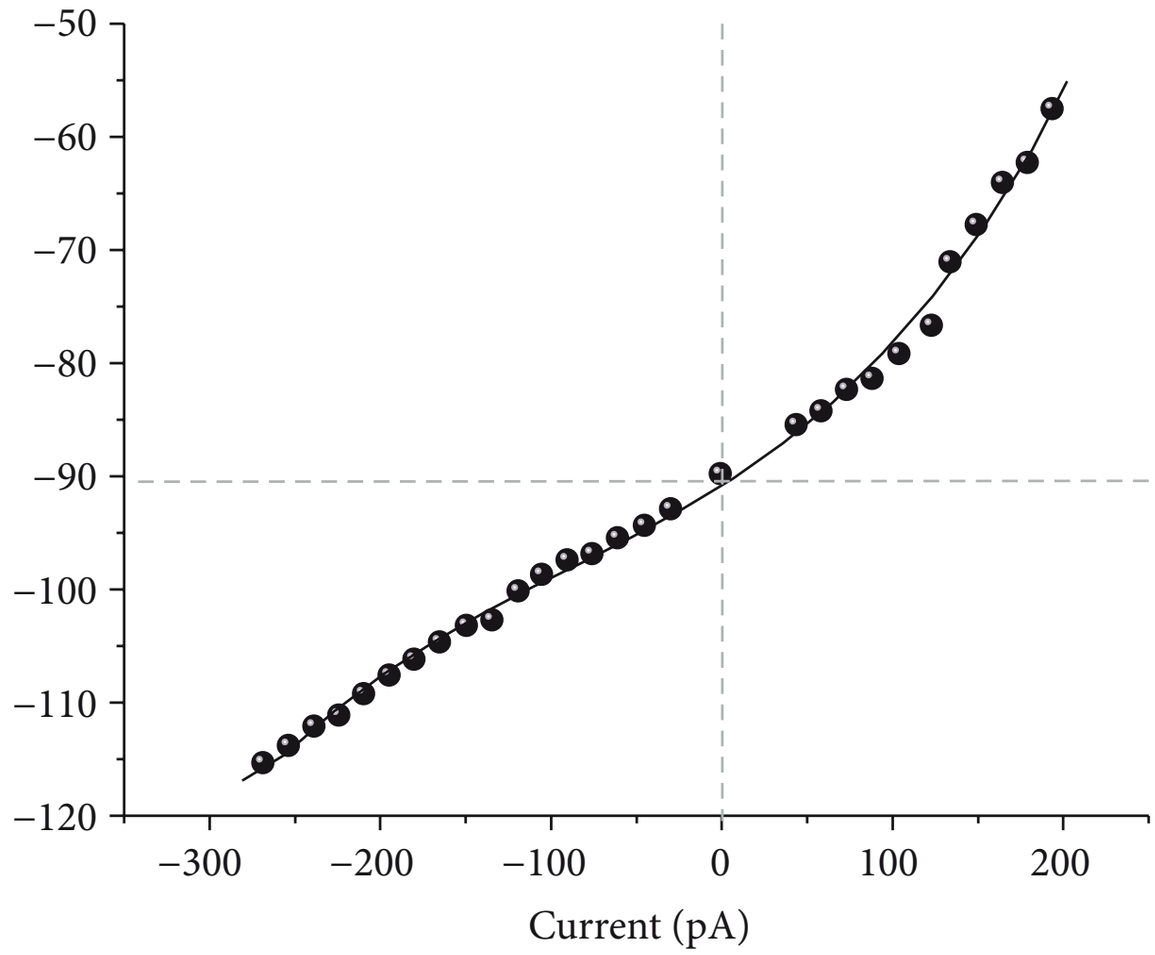
$$\partial_t x = x\frac{x_\infty - x}{\tau_x} - pxh \quad (4)$$

where h is equivalent to the time step in the time series, l is the cooperativity of calcium for the increase in the probability of release.

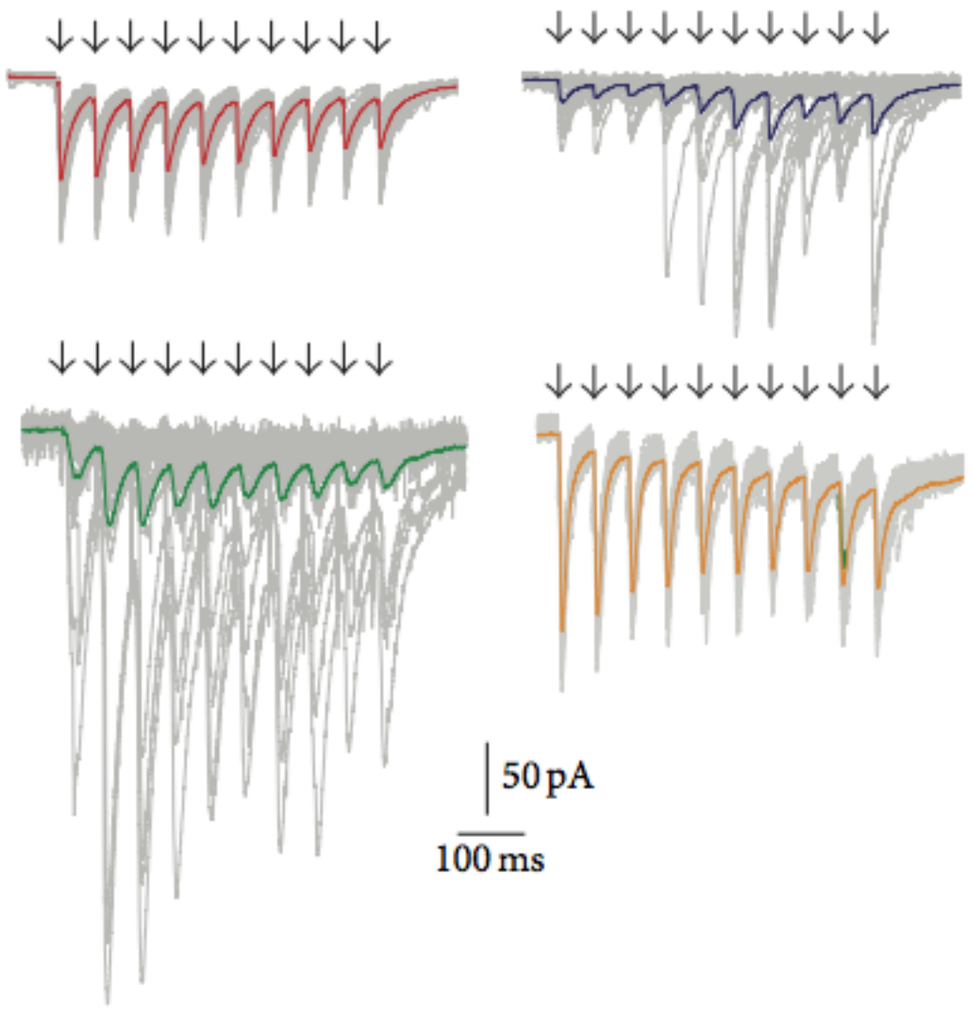
Long range interneurons enable communication between local networks in the striatum




25 mV
200 pA
100 ms

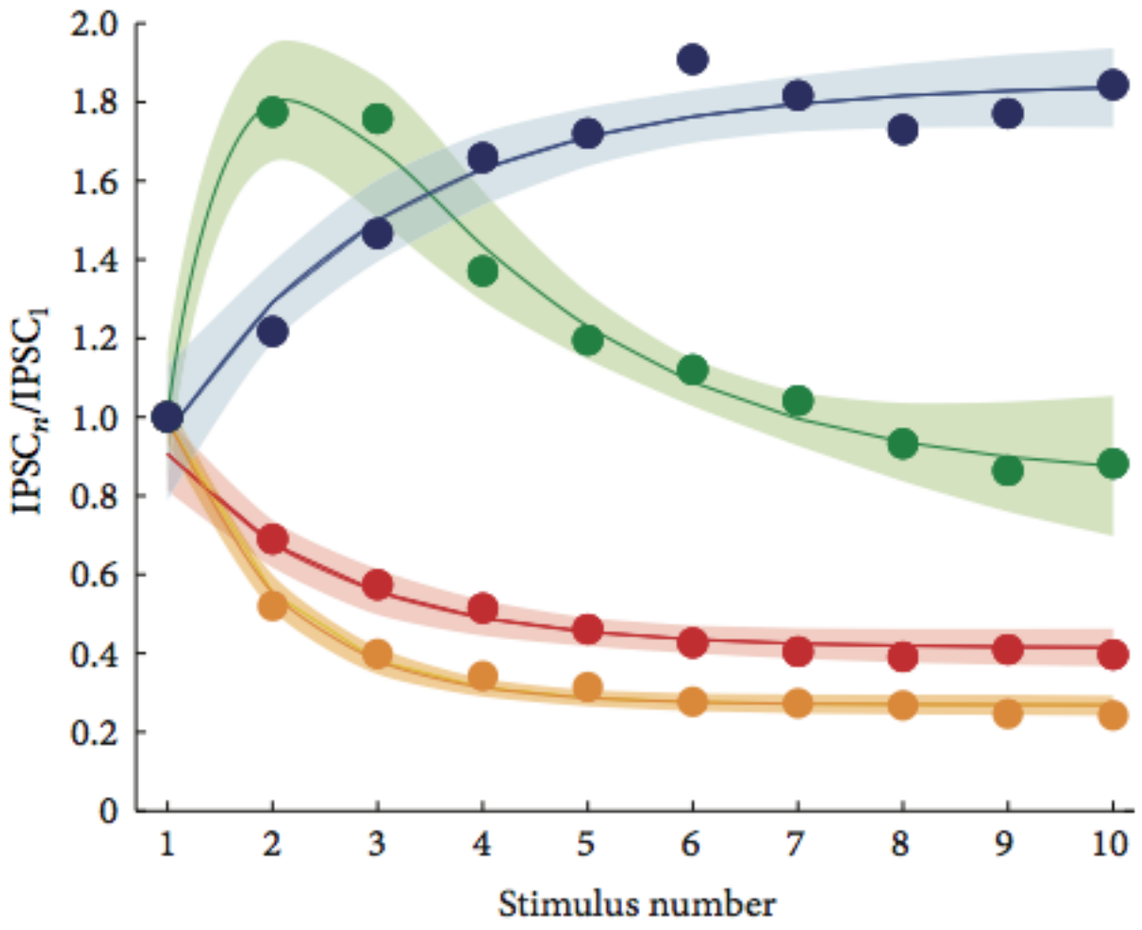

−50
−60
−70
−80
−90
−100
−110
−120
Voltage (mV)
−300
−200
−100
0
100
200
Current (pA)

(a)

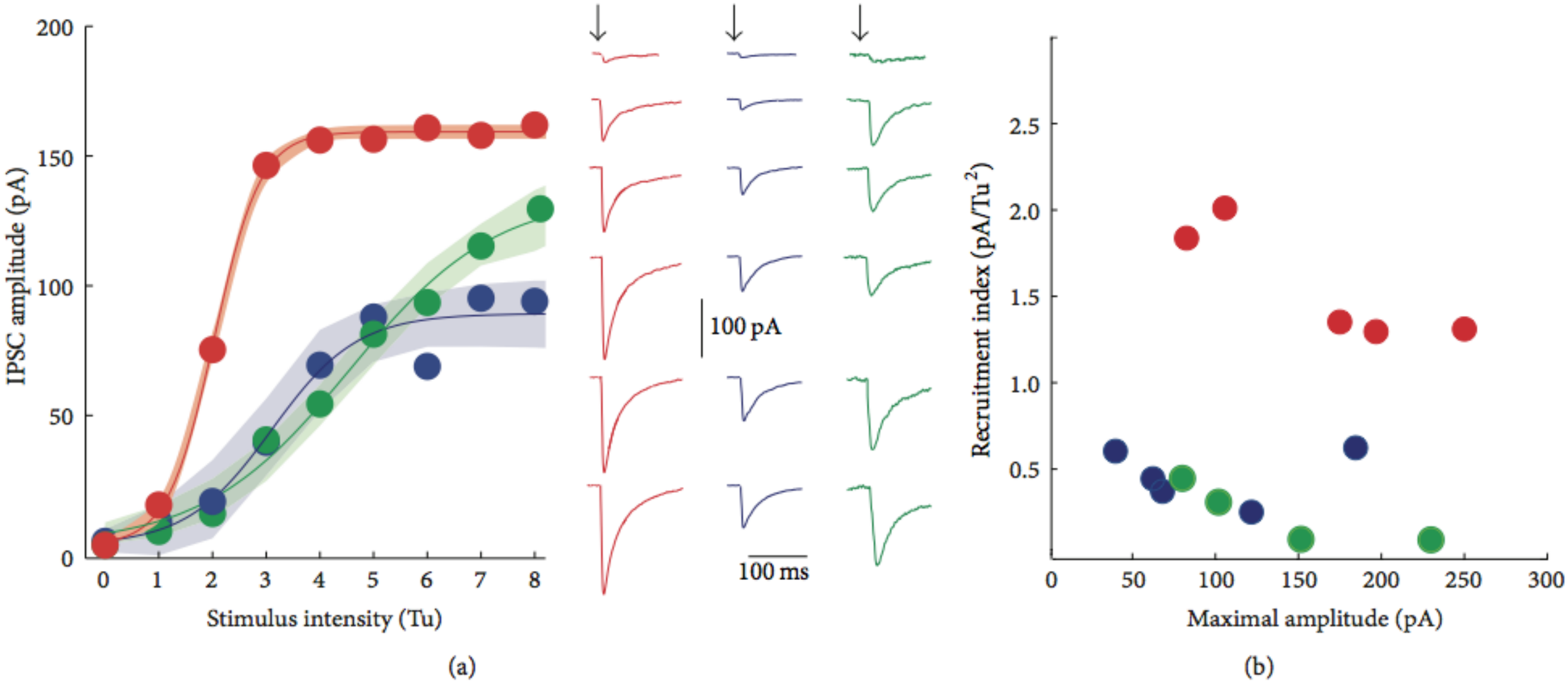

50 pA
100 ms

(c)

(b)

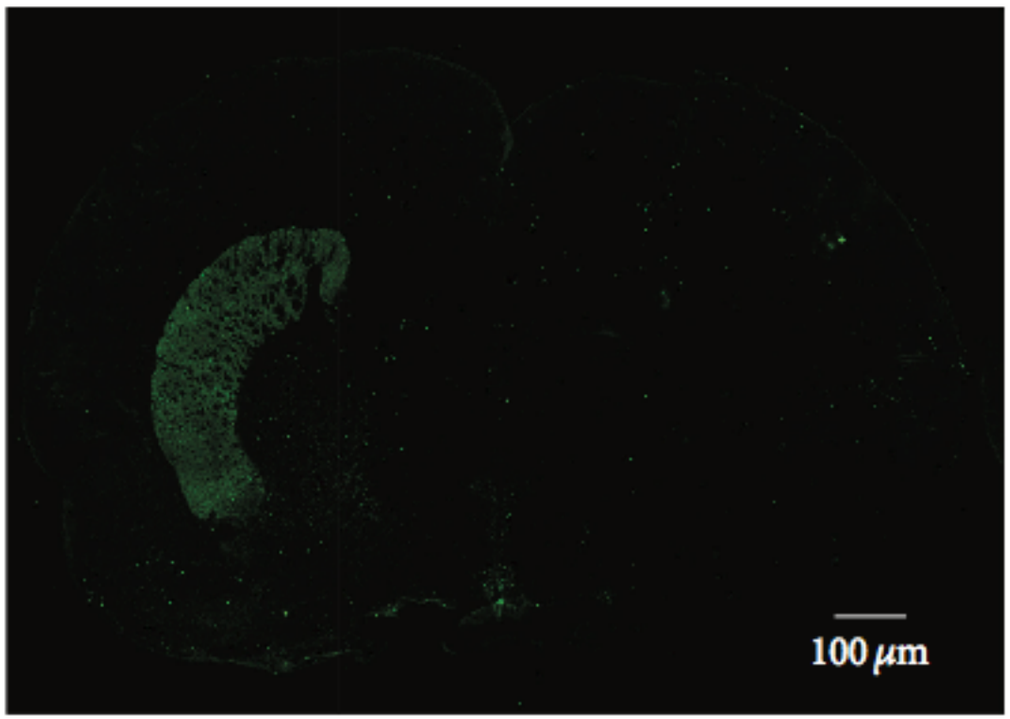

IPSC$_n$/IPSC$_1$
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
10
Stimulus number

(d)

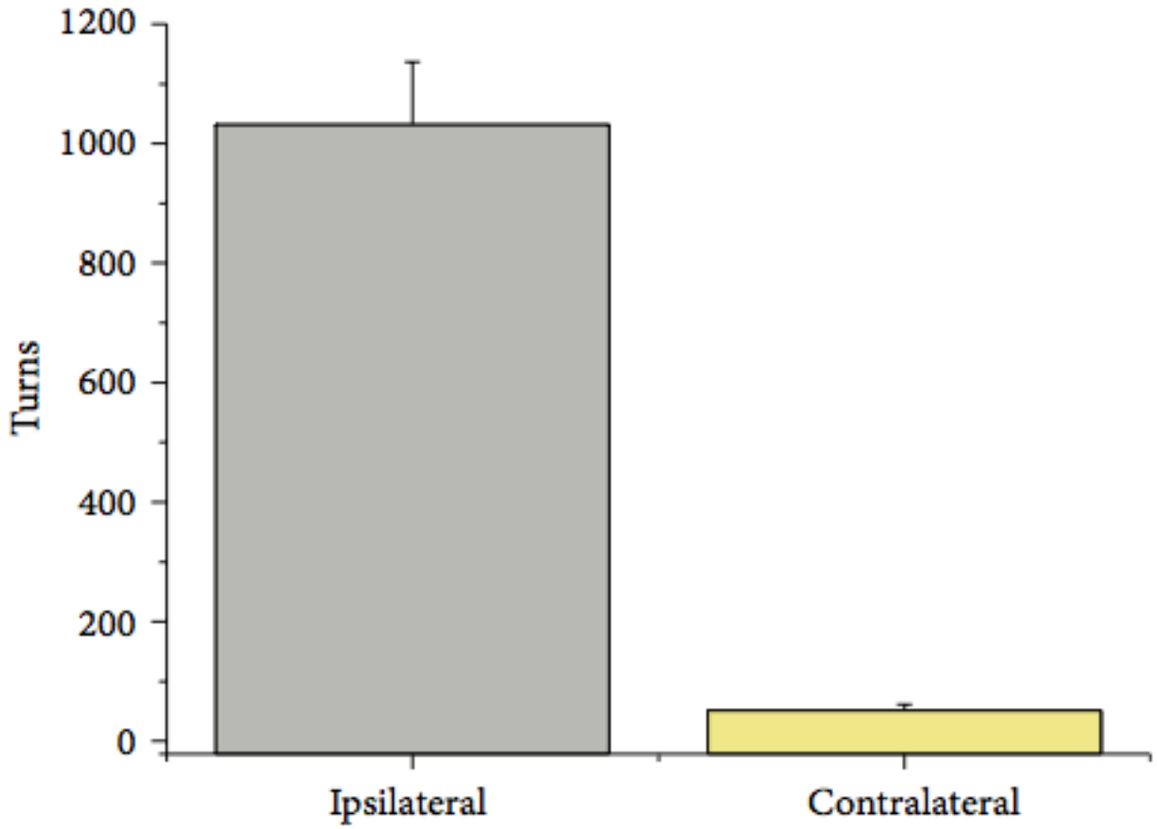

IPSC amplitude (pA)
200
150
100
50
0
0
1
2
3
4
5
6
7
8
Stimulus intensity (Tu)
100 pA
100 ms
Recruitment index (pA/Tu²)
2.5
2.0
1.5
1.0
0.5
0
50
100
150
200
250
300
Maximal amplitude (pA)

(a)

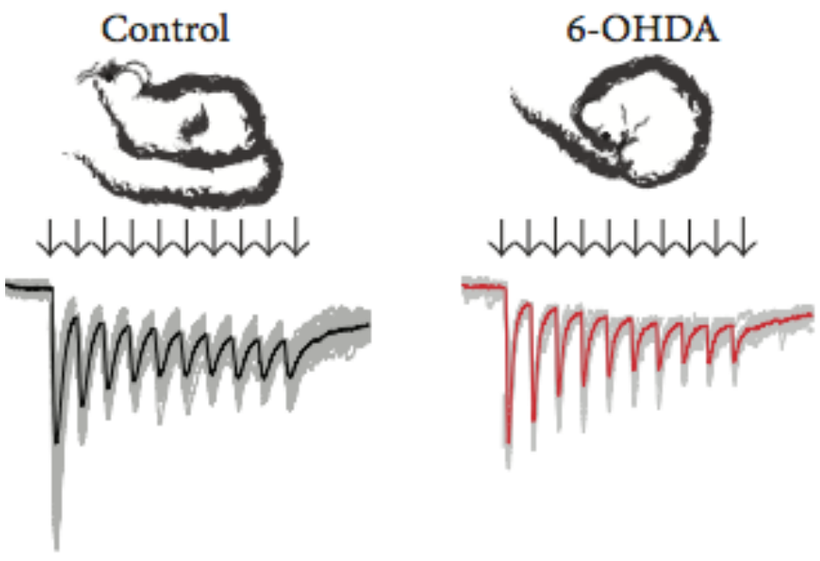
(b)


100 μm

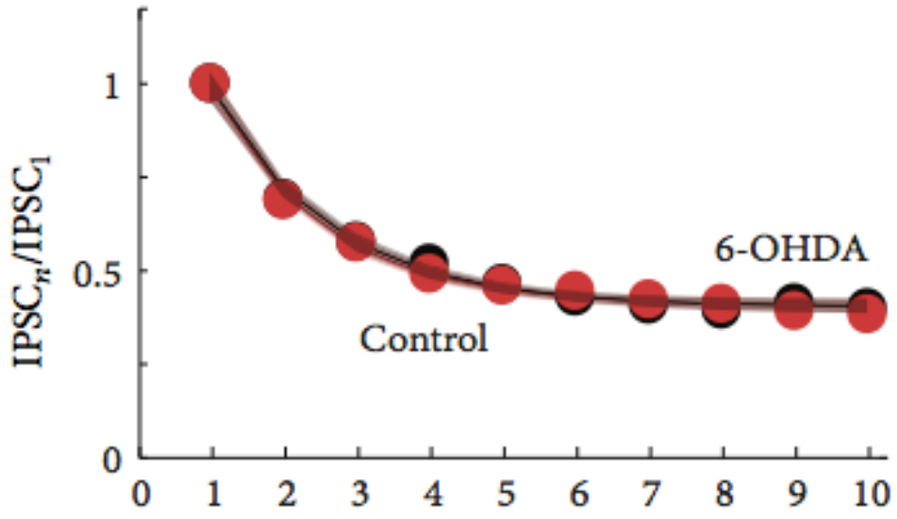
(a)


1200
1000
800
600
400
200
0
Turns
Ipsilateral
Contralateral

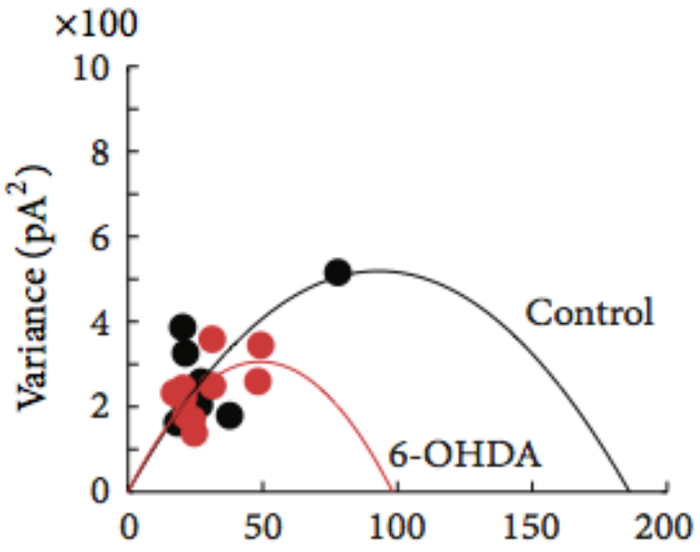
(b)


Control
6-OHDA

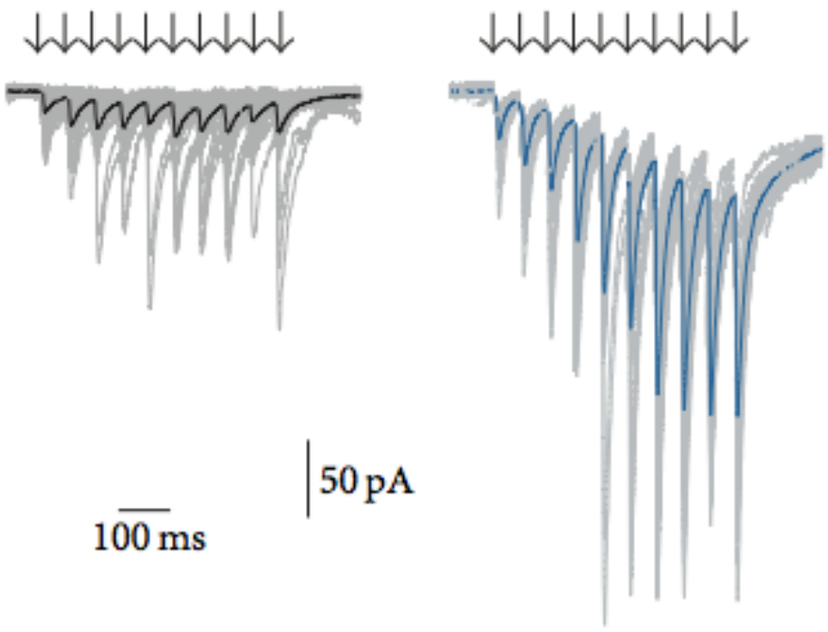
(a)


IPSC$_n$/IPSC$_1$
1
0.5
0
0 1 2 3 4 5 6 7 8 9 10
Control
6-OHDA

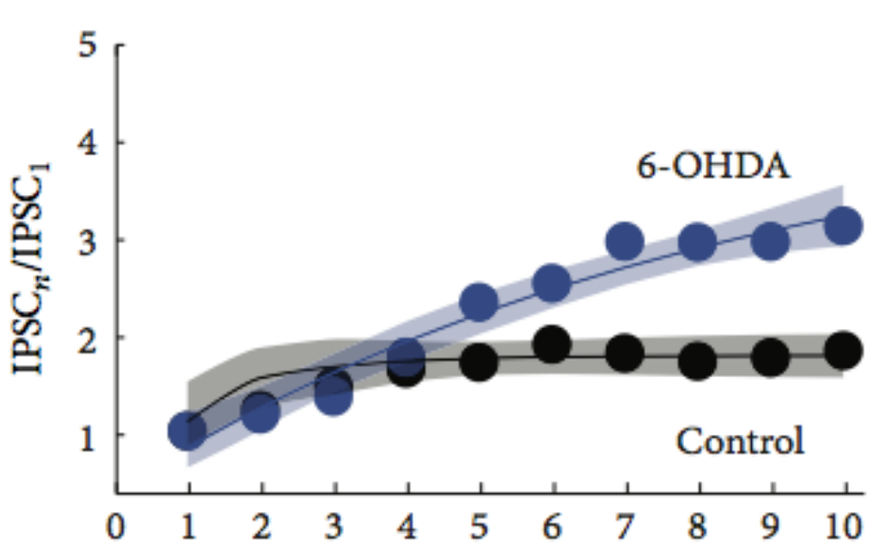
(b)


×100
10
8
6
4
2
0
Variance (pA^2)
0 50 100 150 200
Control
6-OHDA

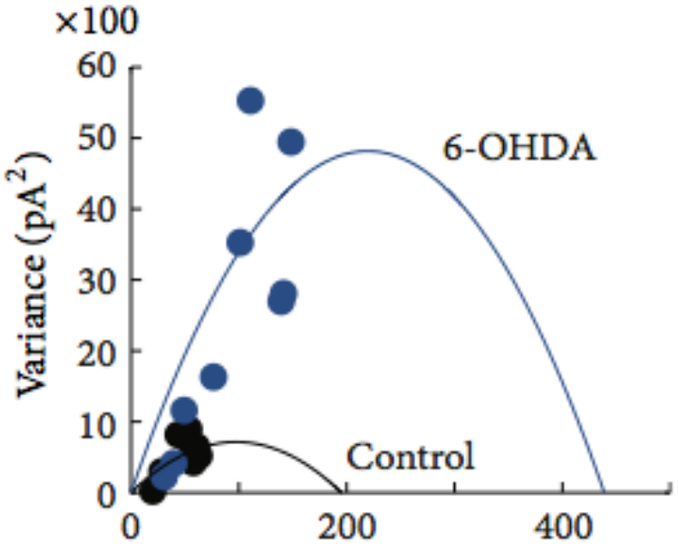
(c)


50 pA
100 ms

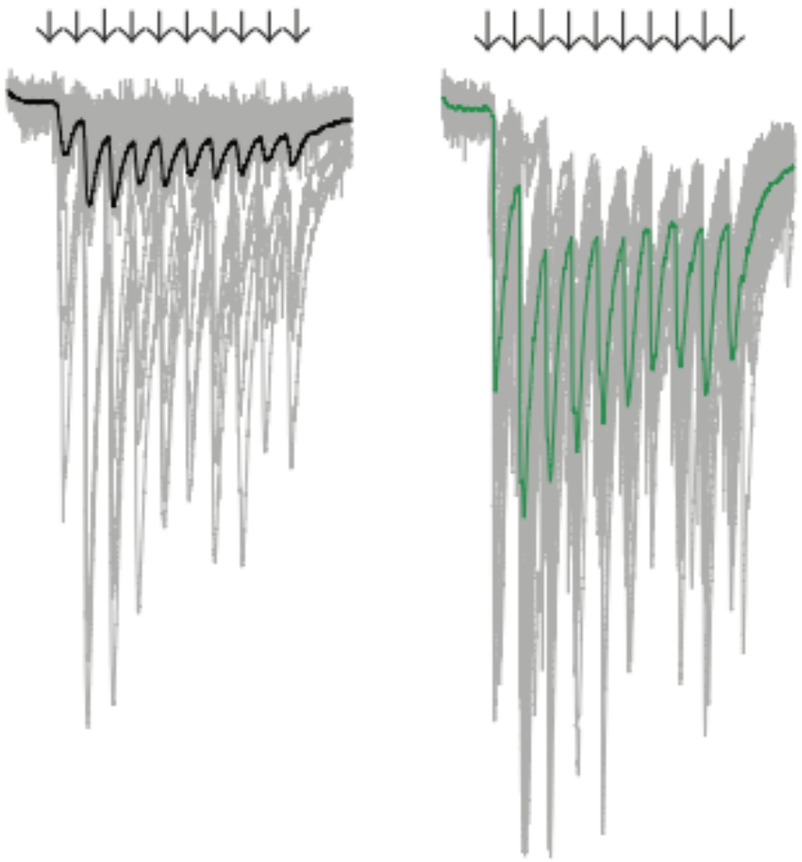
(d)


IPSC$_n$/IPSC$_1$
6-OHDA
Control
0
1
2
3
4
5
6
7
8
9
10

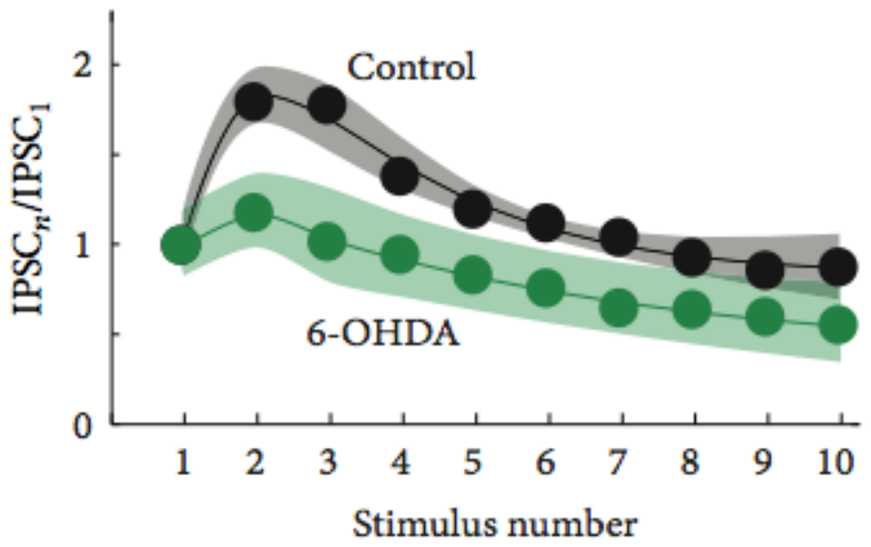
(e)


×100
Variance (pA^2)
6-OHDA
Control
0
10
20
30
40
50
60
200
400

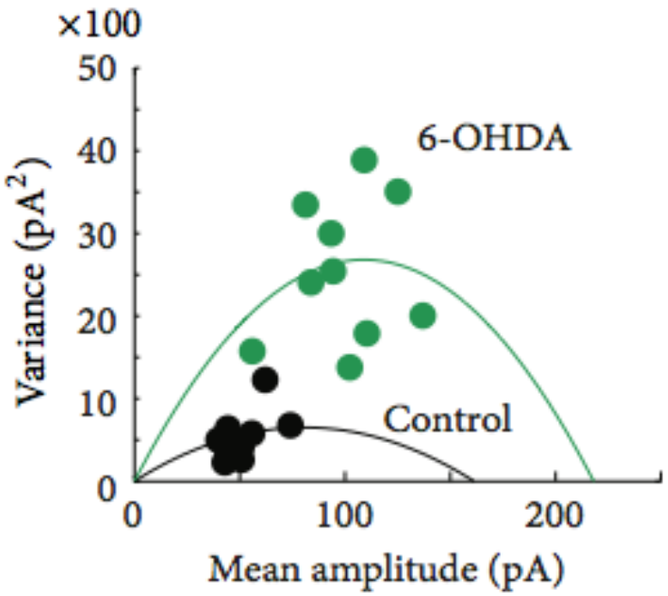
(f)



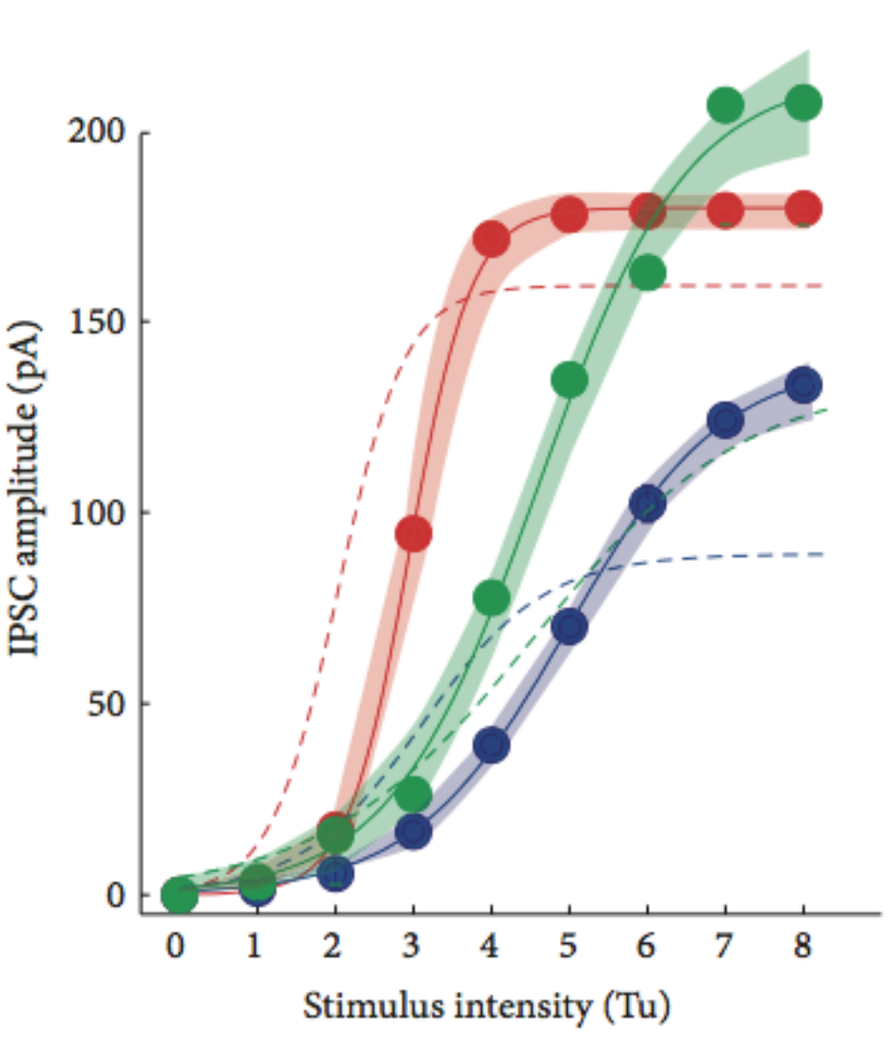
(g)


Control
6-OHDA
IPSC$_n$/IPSC$_1$
Stimulus number

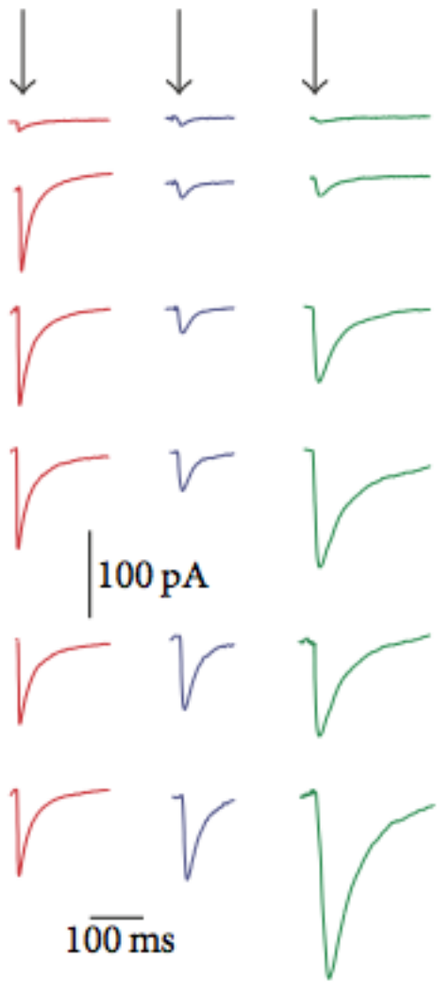
(h)

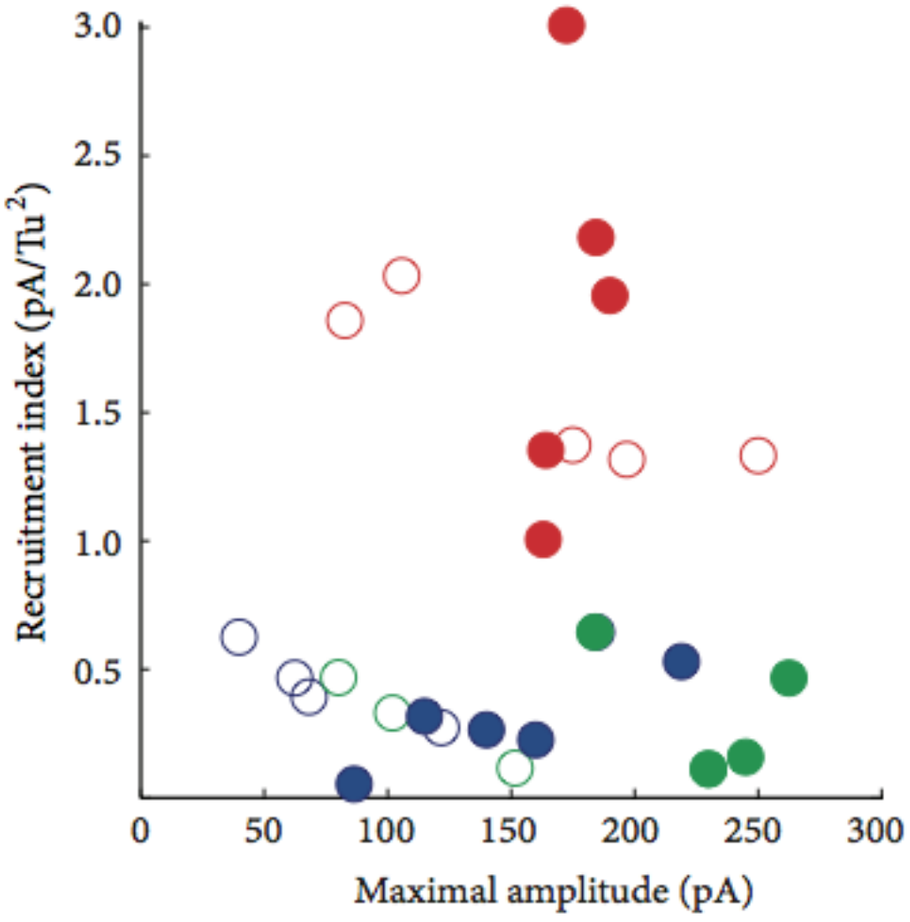

×100
6-OHDA
Control
Variance (pA^2)
Mean amplitude (pA)

(i)

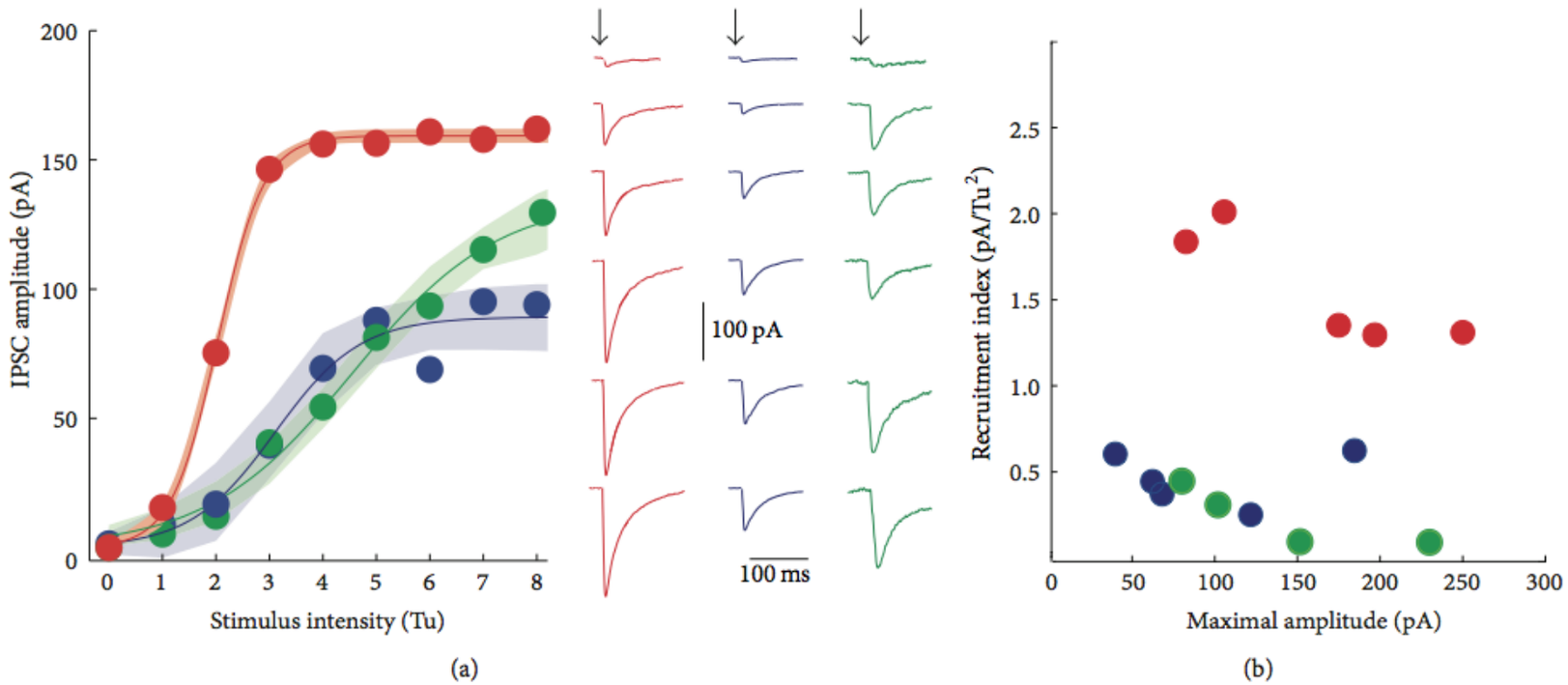

IPSC amplitude (pA)
200
150
100
50
0
0
1
2
3
4
5
6
7
8
Stimulus intensity (Tu)

(a)

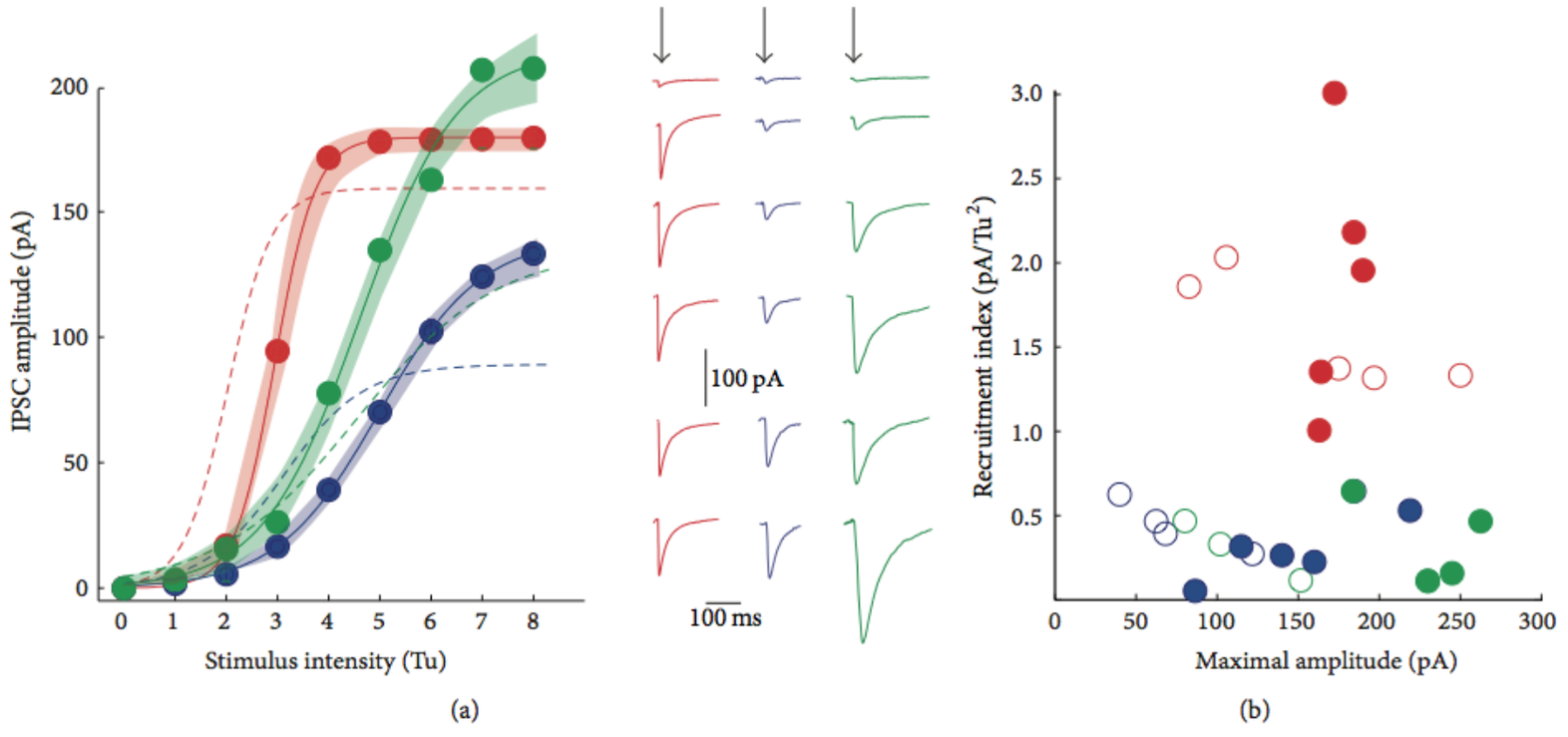

100 pA
100 ms


Recruitment index (pA/Tu^2)
3.0
2.5
2.0
1.5
1.0
0.5
0
50
100
150
200
250
300
Maximal amplitude (pA)

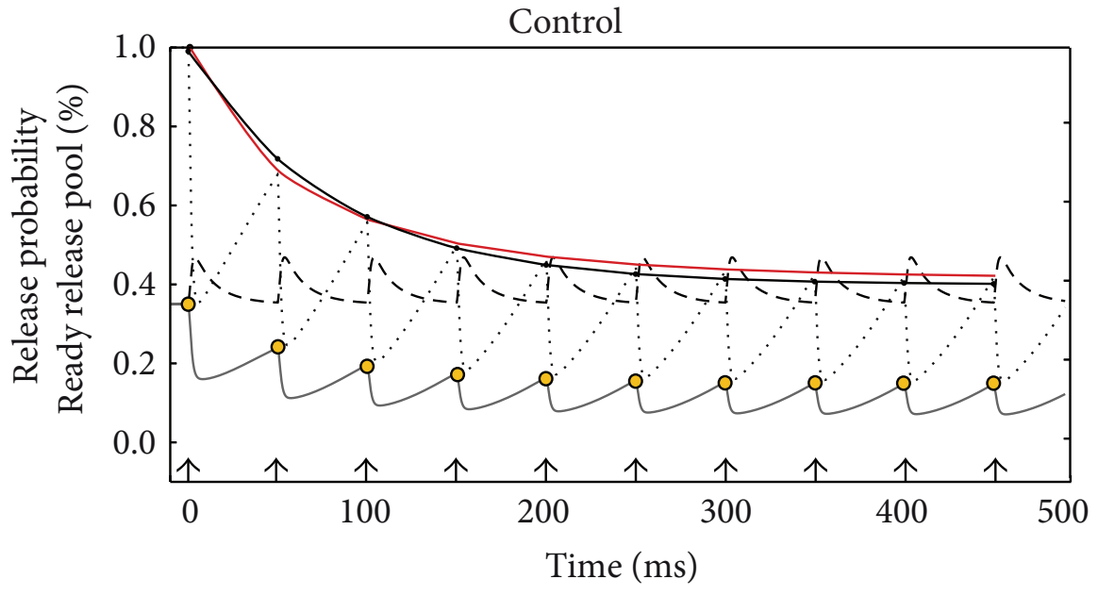
(b)

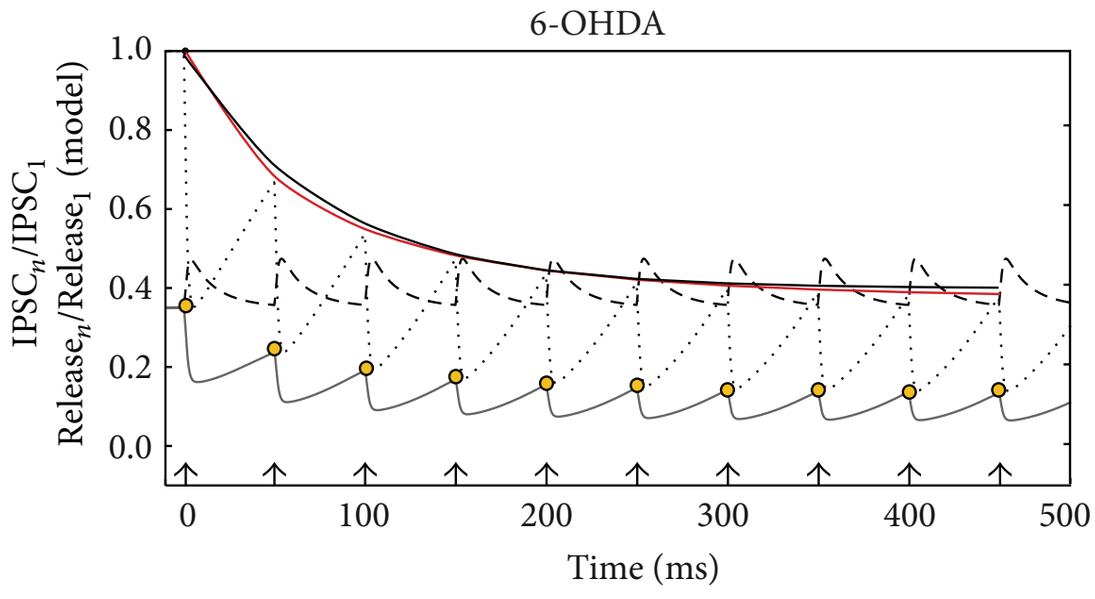

IPSC amplitude (pA)
200
150
100
50
0
0 1 2 3 4 5 6 7 8
Stimulus intensity (Tu)
100 pA
100 ms
Recruitment index (pA/Tu^2)
2.5
2.0
1.5
1.0
0.5
0 50 100 150 200 250 300
Maximal amplitude (pA)

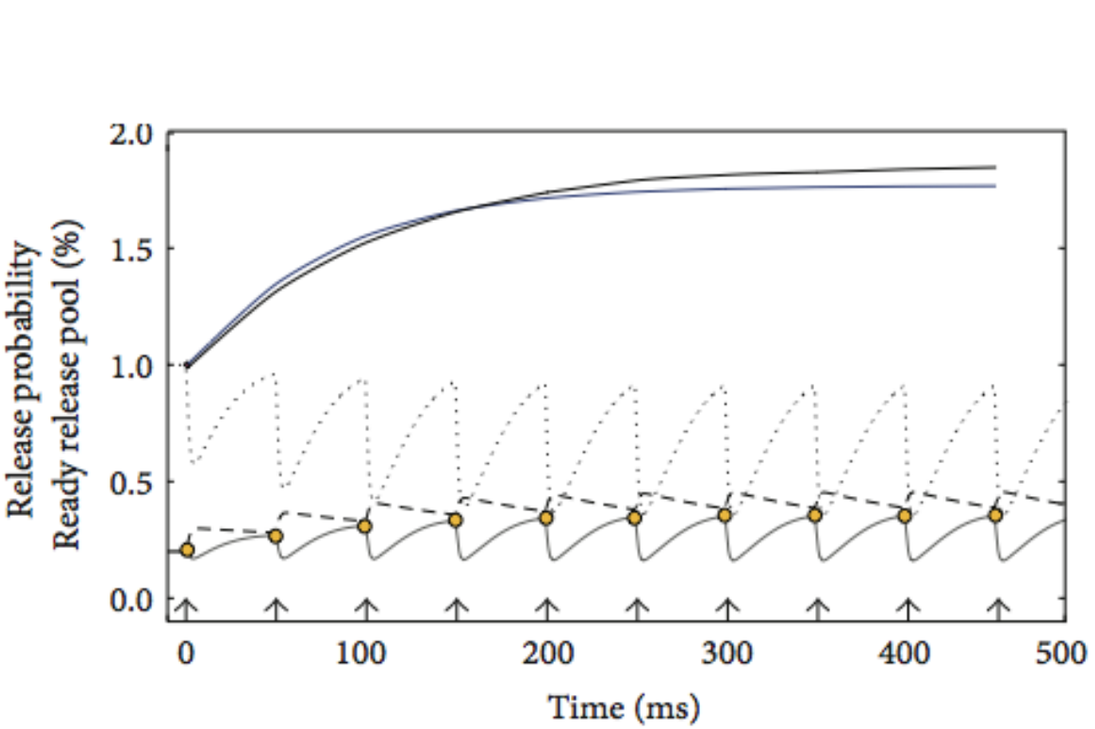
(a) (b)

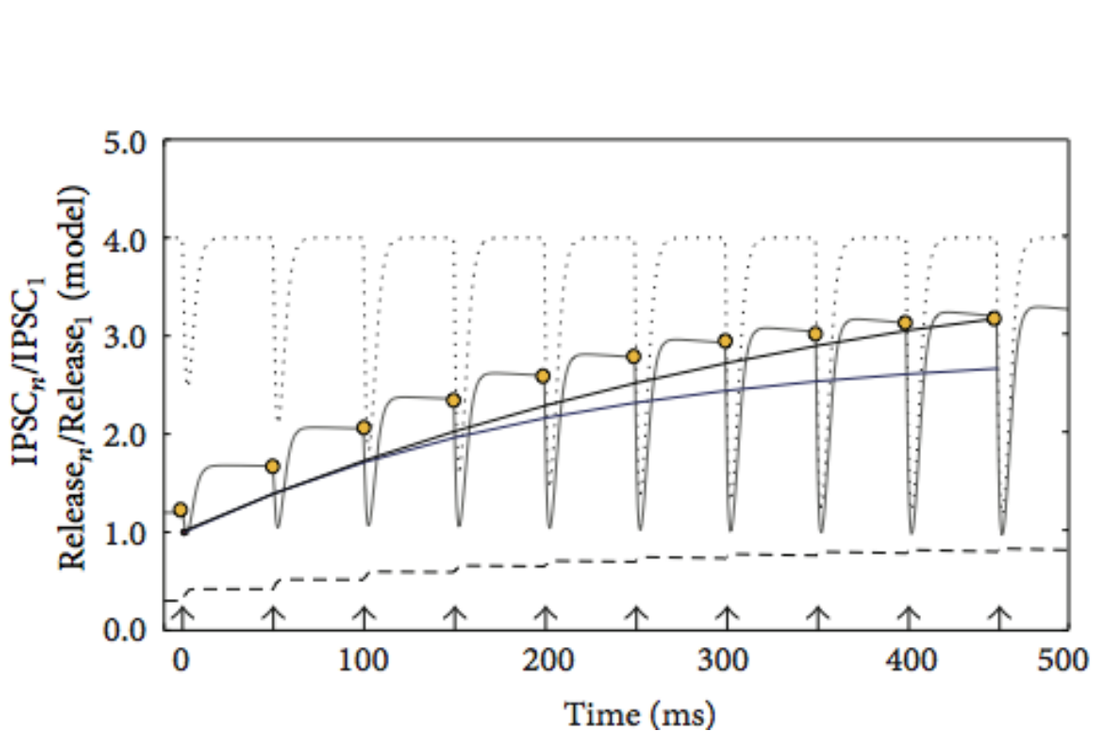

IPSC amplitude (pA)
200
150
100
50
0
0 1 2 3 4 5 6 7 8
Stimulus intensity (Tu)
100 pA
100 ms
Recruitment index (pA/Tu^2)
3.0
2.5
2.0
1.5
1.0
0.5
0 50 100 150 200 250 300
Maximal amplitude (pA)

(a) (b)


Control
Release probability
Ready release pool (%)
1.0
0.8
0.6
0.4
0.2
0.0
0
100
200
300
400
500
Time (ms)


6-OHDA
IPSC$_n$/IPSC$_1$
Release$_n$/Release$_1$ (model)
1.0
0.8
0.6
0.4
0.2
0.0
0
100
200
300
400
500
Time (ms)


Release probability
Ready release pool (%)
2.0
1.5
1.0
0.5
0.0
0
100
200
300
400
500
Time (ms)


IPSC$_n$/IPSC$_1$
Release$_n$/Release$_1$ (model)
5.0
4.0
3.0
2.0
1.0
0.0
0
100
200
300
400
500
Time (ms)

Control

Release probability
Ready release pool (%)

1.0
0.8
0.6
0.4
0.2
0.0

0 100 200 300 400 500

Time (ms)

6-OHDA

$IPSC_n/IPSC_1$
$Release_n/Release_1$ (model)

1.0
0.8
0.6
0.4
0.2
0.0

0 100 200 300 400 500

Time (ms)

Release probability
Ready release pool (%)

2.0
1.5
1.0
0.5
0.0

0 100 200 300 400 500

Time (ms)

$IPSC_n/IPSC_1$
$Release_n/Release_1$ (model)

5.0
4.0
3.0
2.0
1.0
0.0

0 100 200 300 400 500

Time (ms)

Release probability
Ready release pool (%)

2.0
1.5
1.0
0.5
0.0

0 100 200 300 400 500

Time (ms)

$IPSC_n/IPSC_1$
$Release_n/Release_1$ (model)

1.2
1.0
0.8
0.6
0.4
0.2
0.0

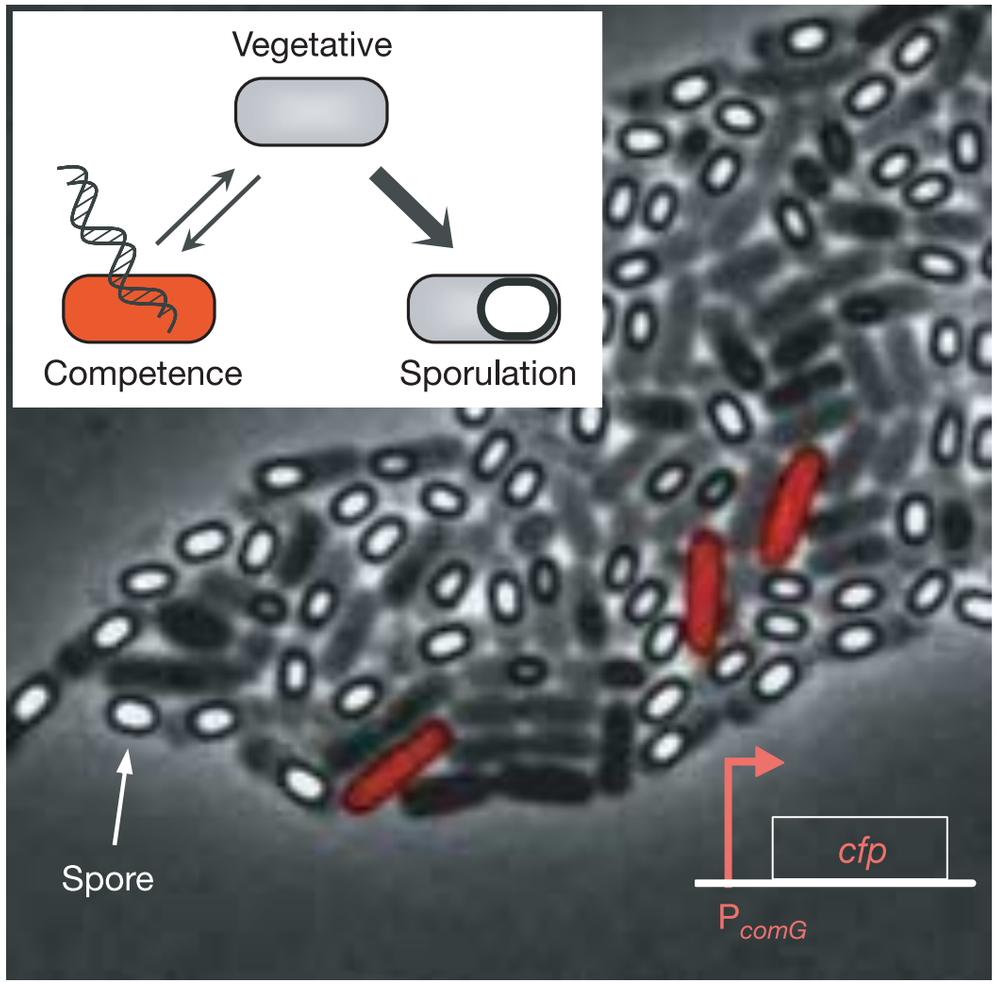
0 100 200 300 400 500

Time (ms)

Cellular differentiation in Bacillus subtilis: Entry into competent states

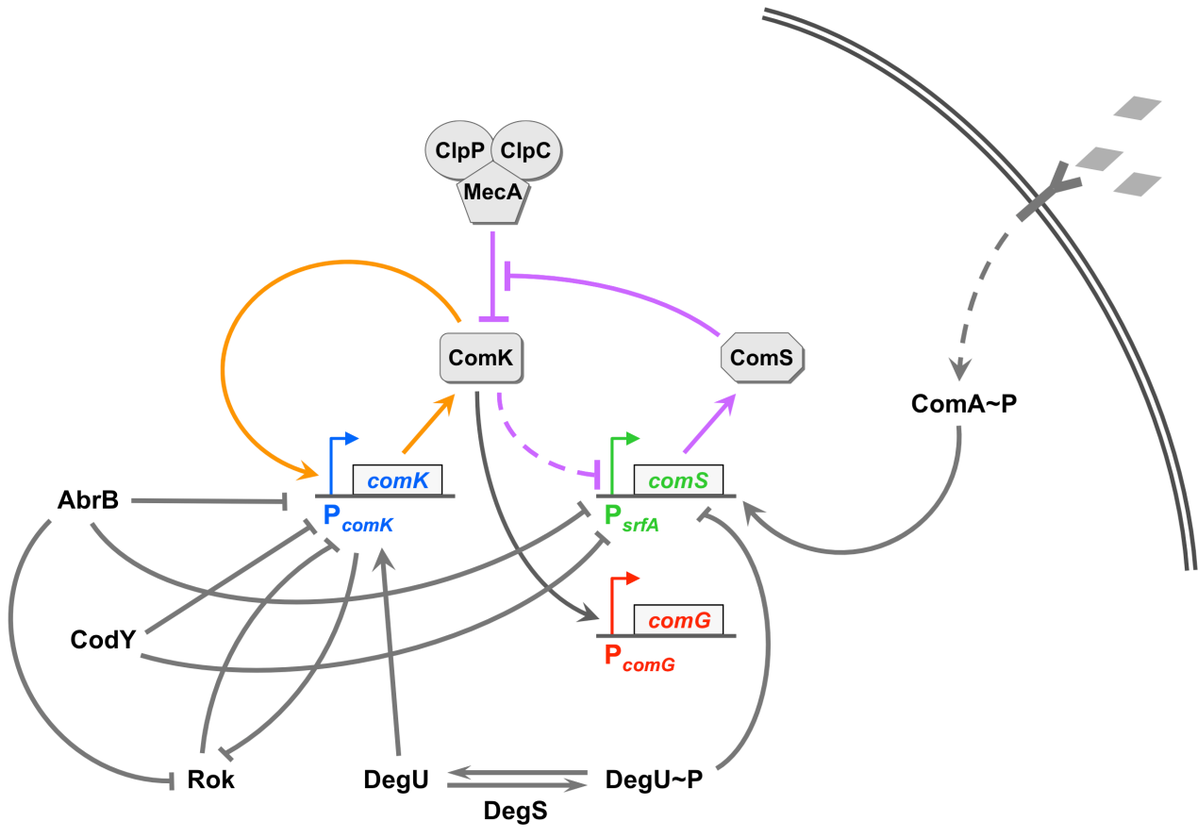
Small percentage of cells enter into competence state in response to nutritional stress

a



From Süel, Garcia-Ojalvo, Liberman & Elowitz, 2006

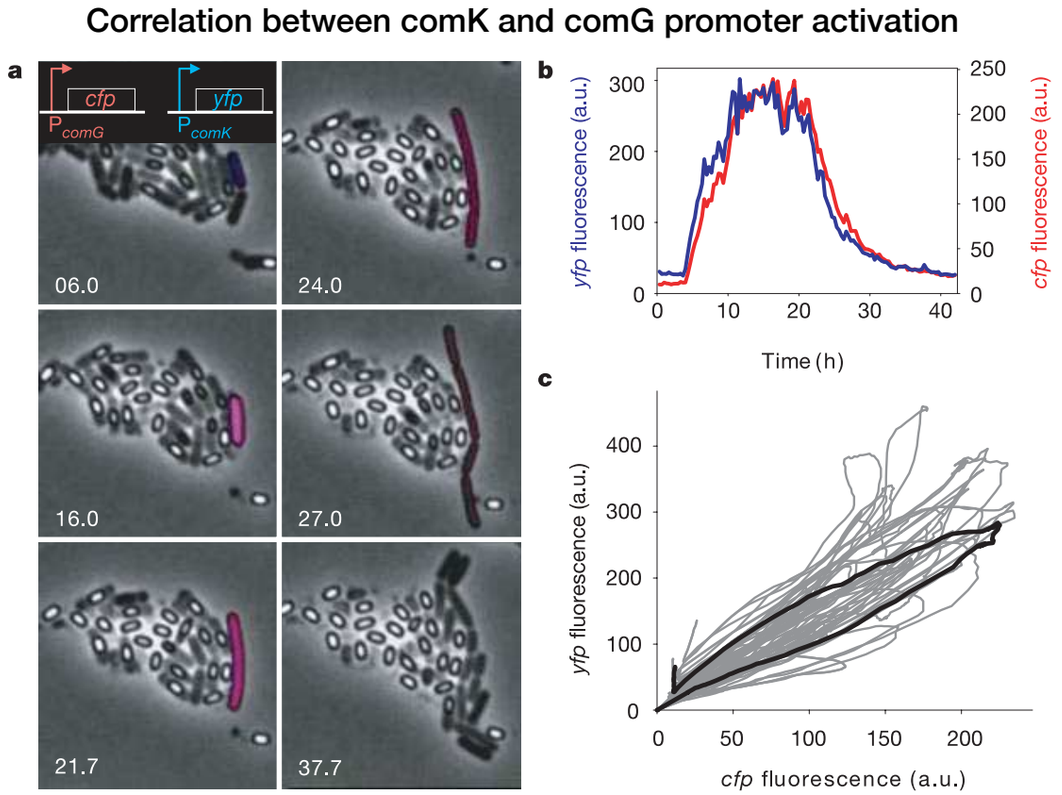
Entry into competence depends on the activation of the promoter of the master regulator gene comK and other network components

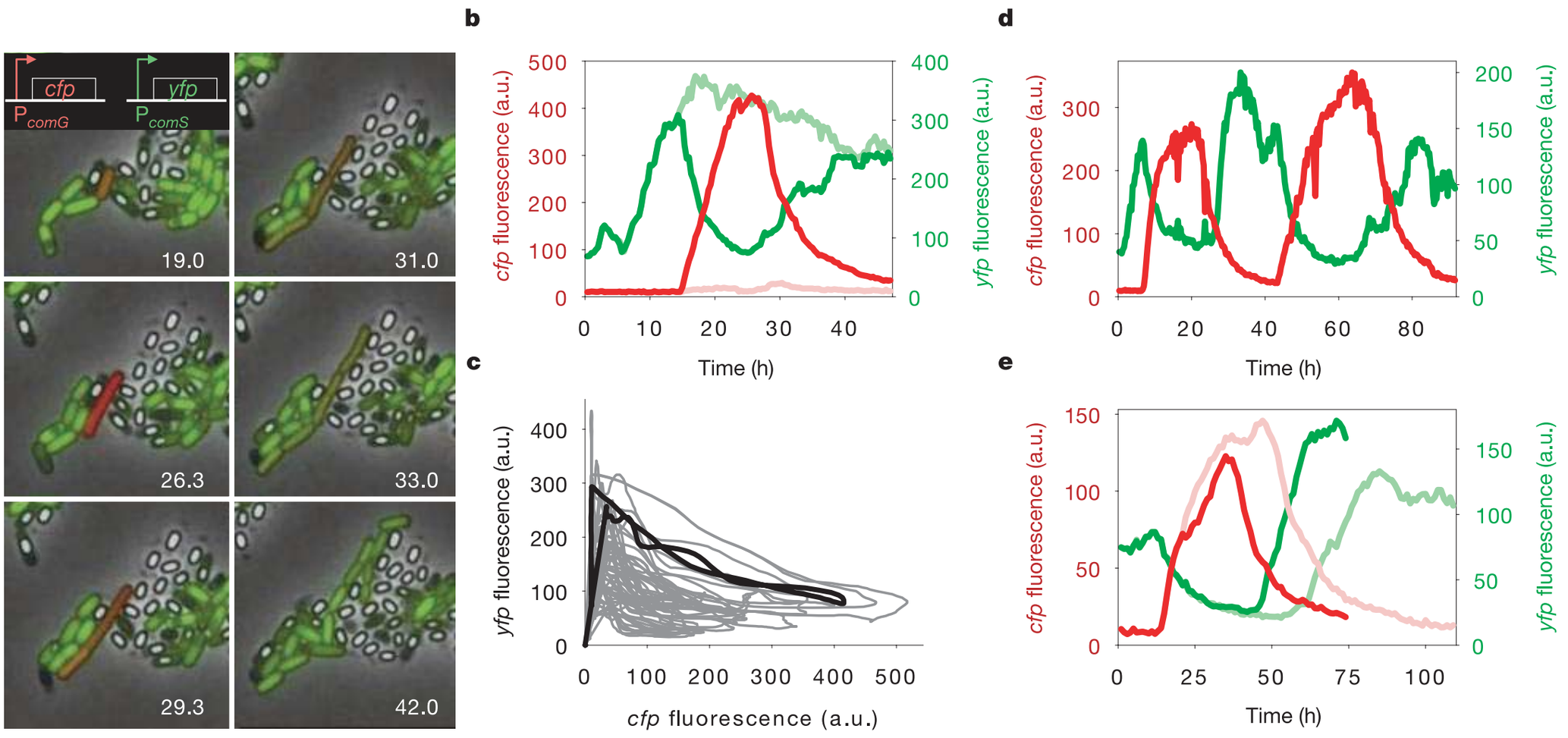


From Süel, et al., 2006

- The activations of the *comK* and *comG* promoters are strongly and positively correlated.

- The activations of the promoters for *comK and comS* *are correlated strongly and negatively*

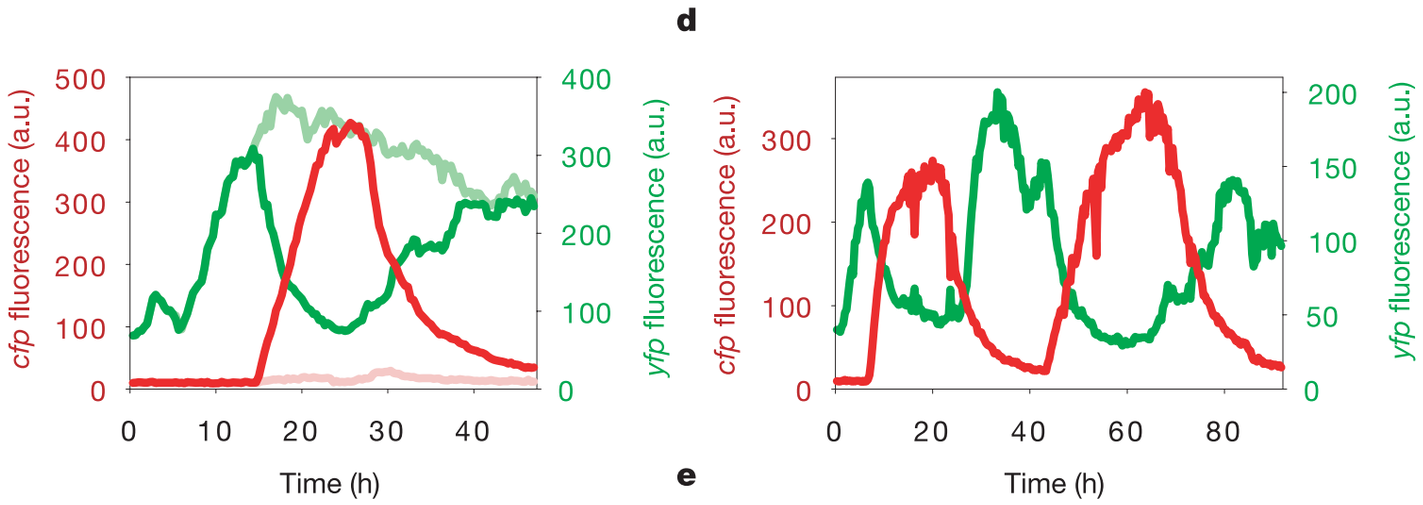




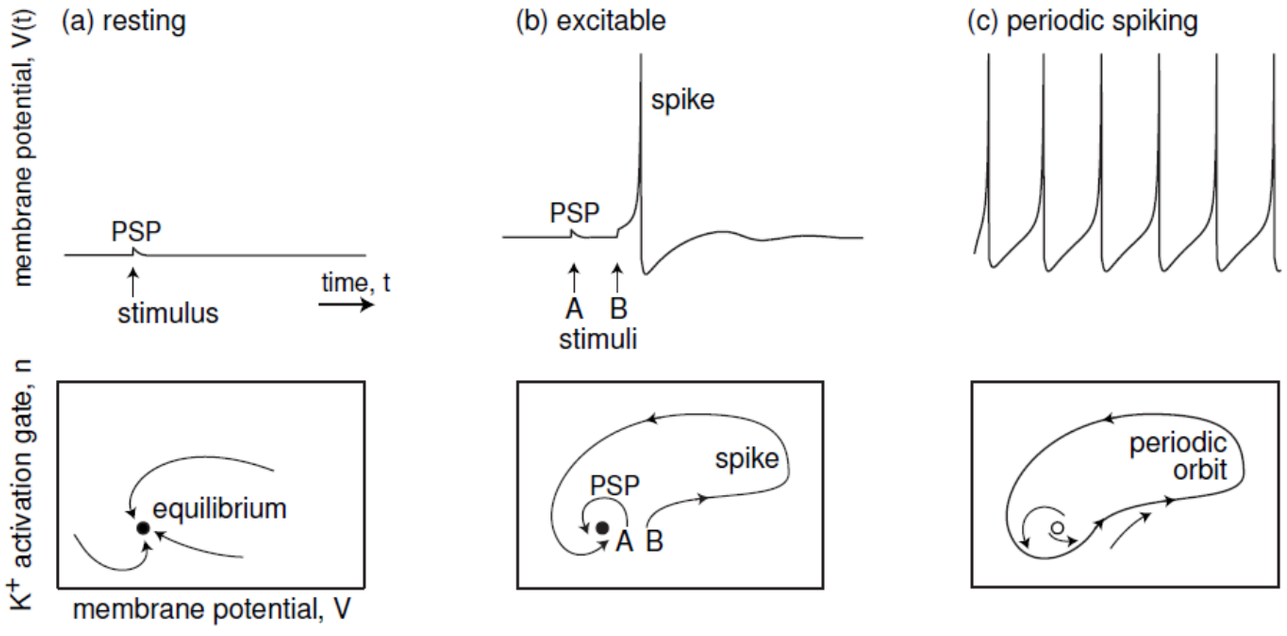
From Süel, et al. 2006

The data shows the first two types of behaviors

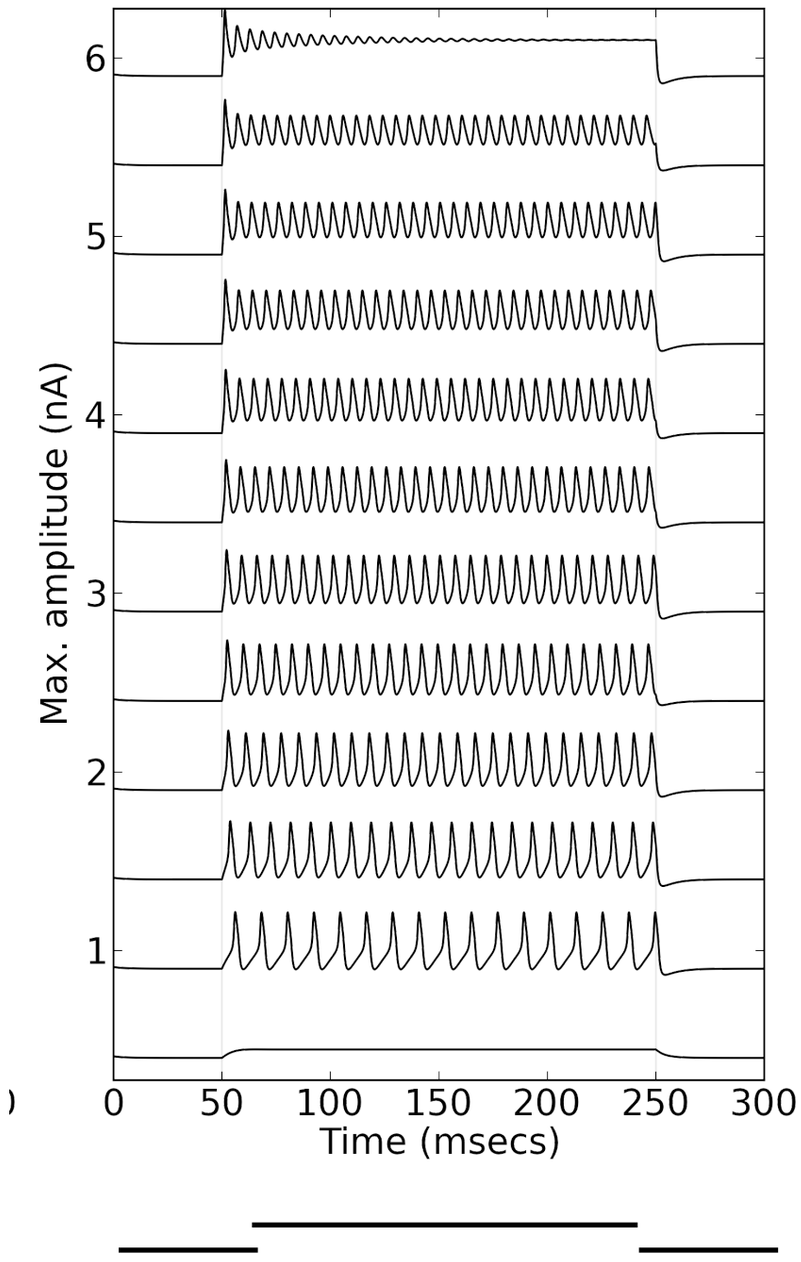
Stable rest and repetitive spiking



From Süel & Elowitz, 2006



Prediction from modeling that is routinely observed in experiments with neurons:
Depolarization block in response to increased current injection in motor neurons. Each trace (in mV) represents a response to current injection.

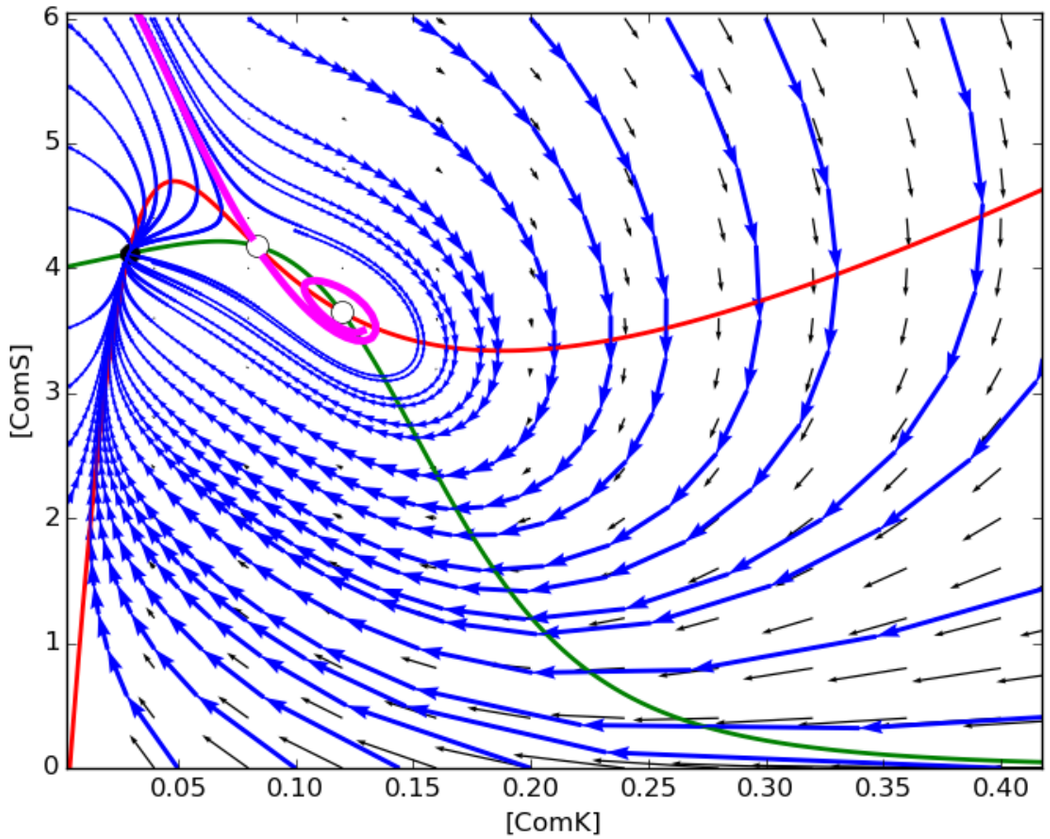


From Herrera-Valdez, 2012

Two of the possible behaviors

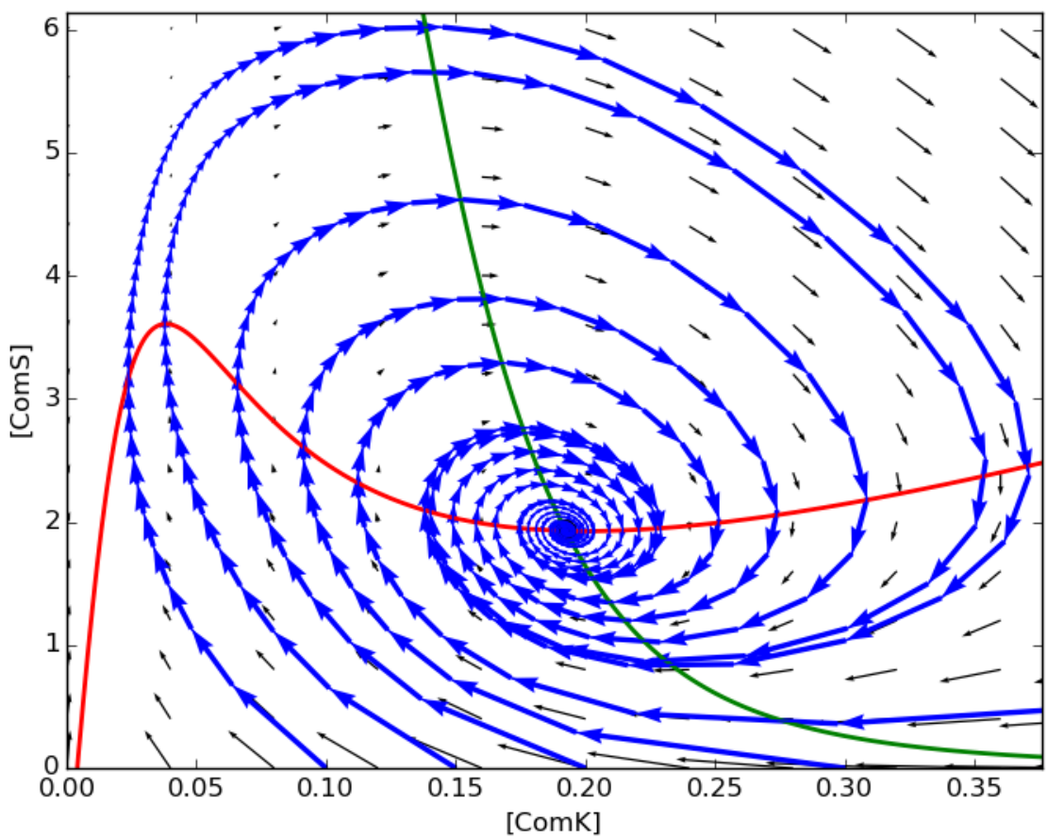
Excitability

Convergence toward a resting concentration of ComK (an attractor fixed point) in two ways:
Large enough perturbations from rest result in transient but large increases in [ComK]. Small perturbations result in short trajectories toward rest.



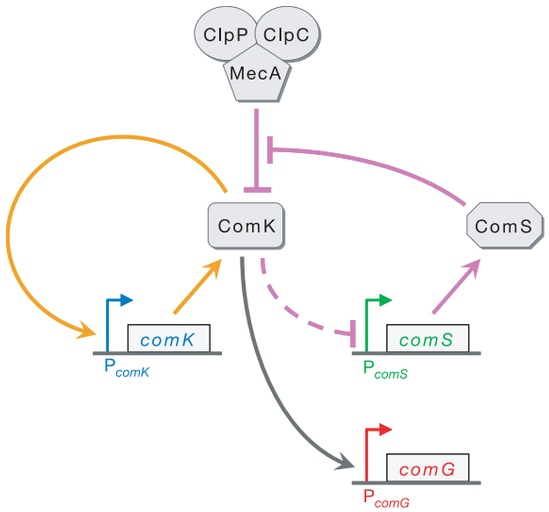
Up-state block

Convergence toward a higher resting level for [ComK] (attractor fixed point).
Small perturbations of the system from rest result in short trajectories. Large enough perturbations result in long excursions (pulsed behavior).



Simulations based on the Süel & Elowitz model, 2006

Interaction between ComK y ComS



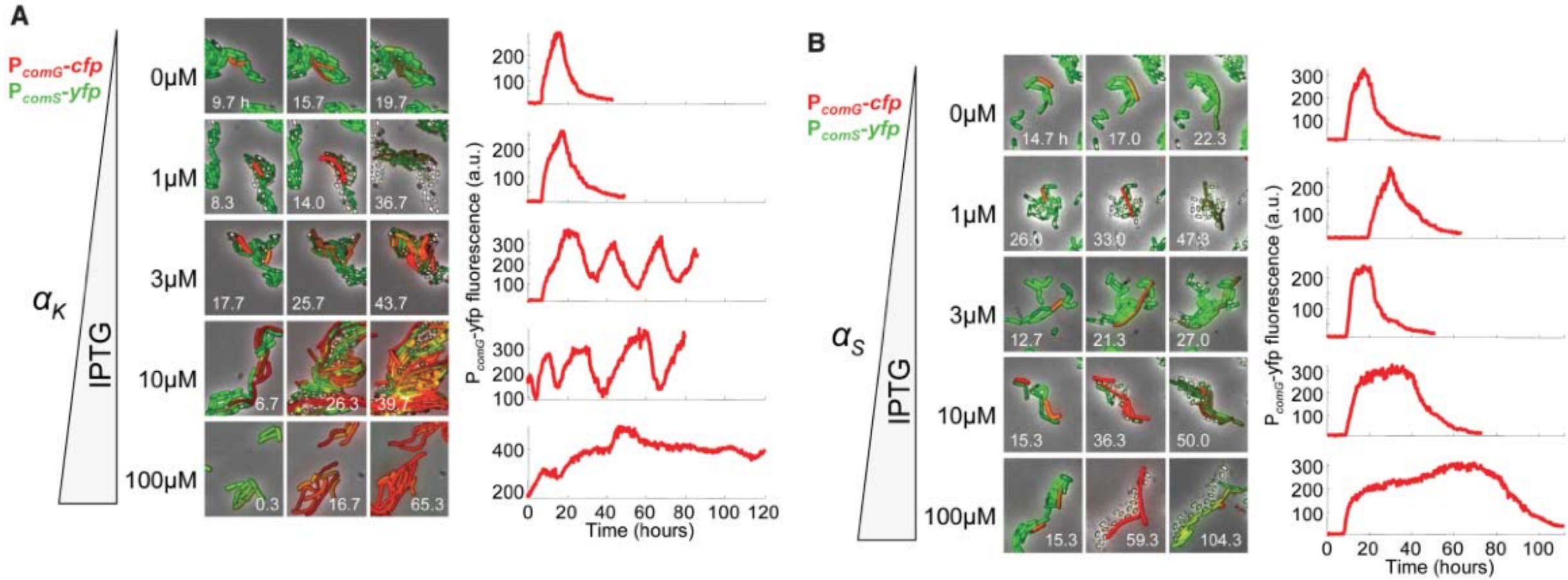
$$\partial_t K = a + \frac{bK^n}{k^n + K^n} - \frac{\mathrm{m}K}{1 + K + S}$$

- $\partial_t K$: time-dependent change in the concentration of ComK
- a: minimal rate of ComK expression
- b: fully activated rate of ComK expression
- n: ComK cooperativity
- k: ComK half-maximum activation rate
- m: ComK degradation in

$$\partial_t S = \frac{c}{h^p + K^p} - \frac{\mathrm{r}\,S}{1 + K + S} + \zeta(t)$$

- $\partial_t S$: time-dependent change in the concentration of ComS
- c: maximum ComS expression rate
- h: ComS half-maximum activation rate
- p: ComK cooperativity
- r: ComS degradation
- $\zeta(t)$: Random fluctuations in ComS

Behaviors predicted by the model can actually be observed in experimentally



Excitability —> Periodic oscillations —> Up-block

2-Dimensional, modified version of the Süel & Elowitz model

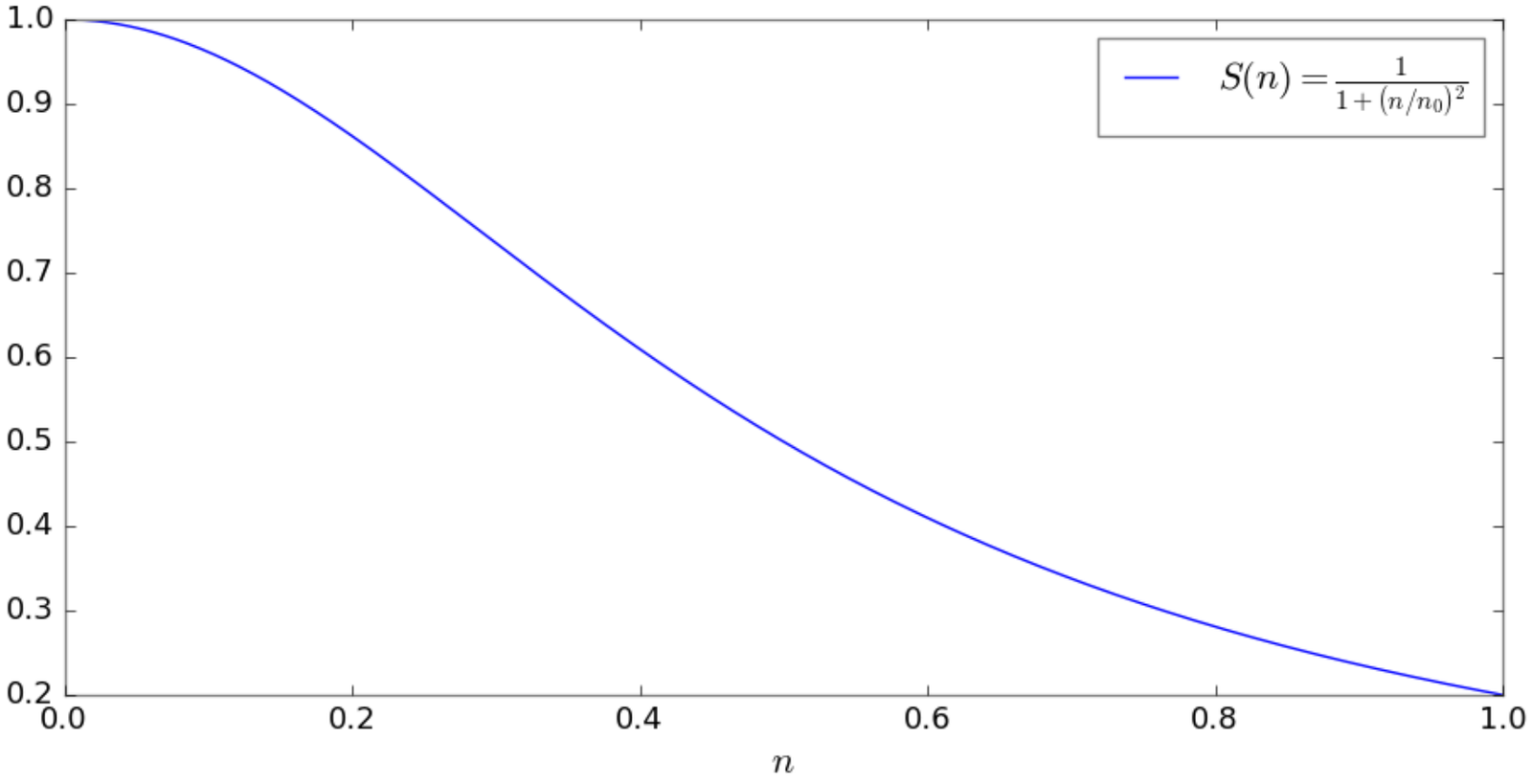
Let x and y represent the concentrations of ComK and ComS, respectively. Assume

$$\partial_t x = a_x + \frac{b_x}{1+(k_x/x)^{c_x}} - \frac{d_x x}{1+\frac{x}{g_x}+\frac{y}{g_y}} \tag{1}$$

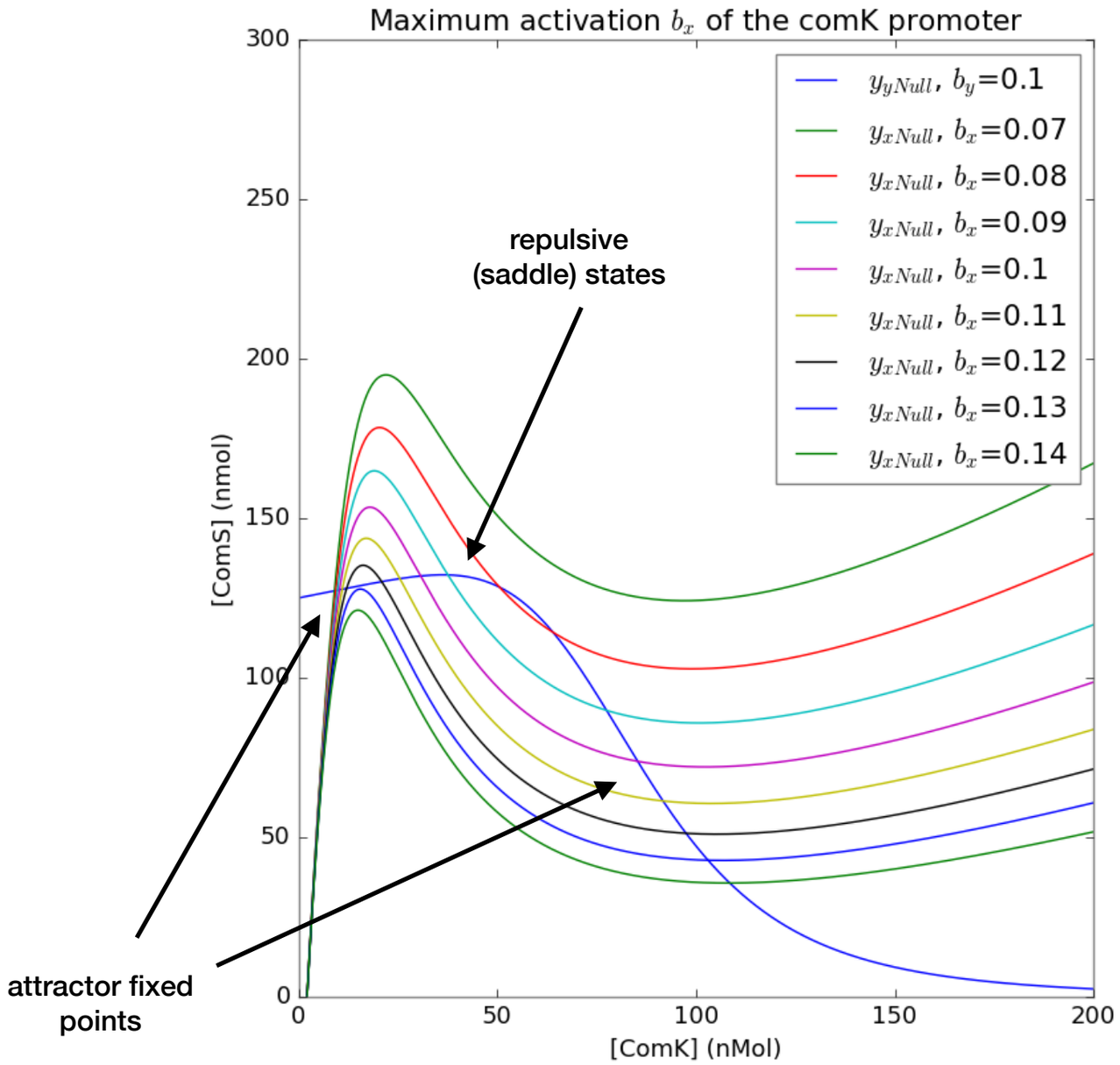
$$\partial_t y = a_s + S(n)\frac{b_y}{1+(x/k_y)^{c_y}} - \frac{d_y y}{1+\frac{x}{g_x}+\frac{y}{g_y}} \tag{2}$$

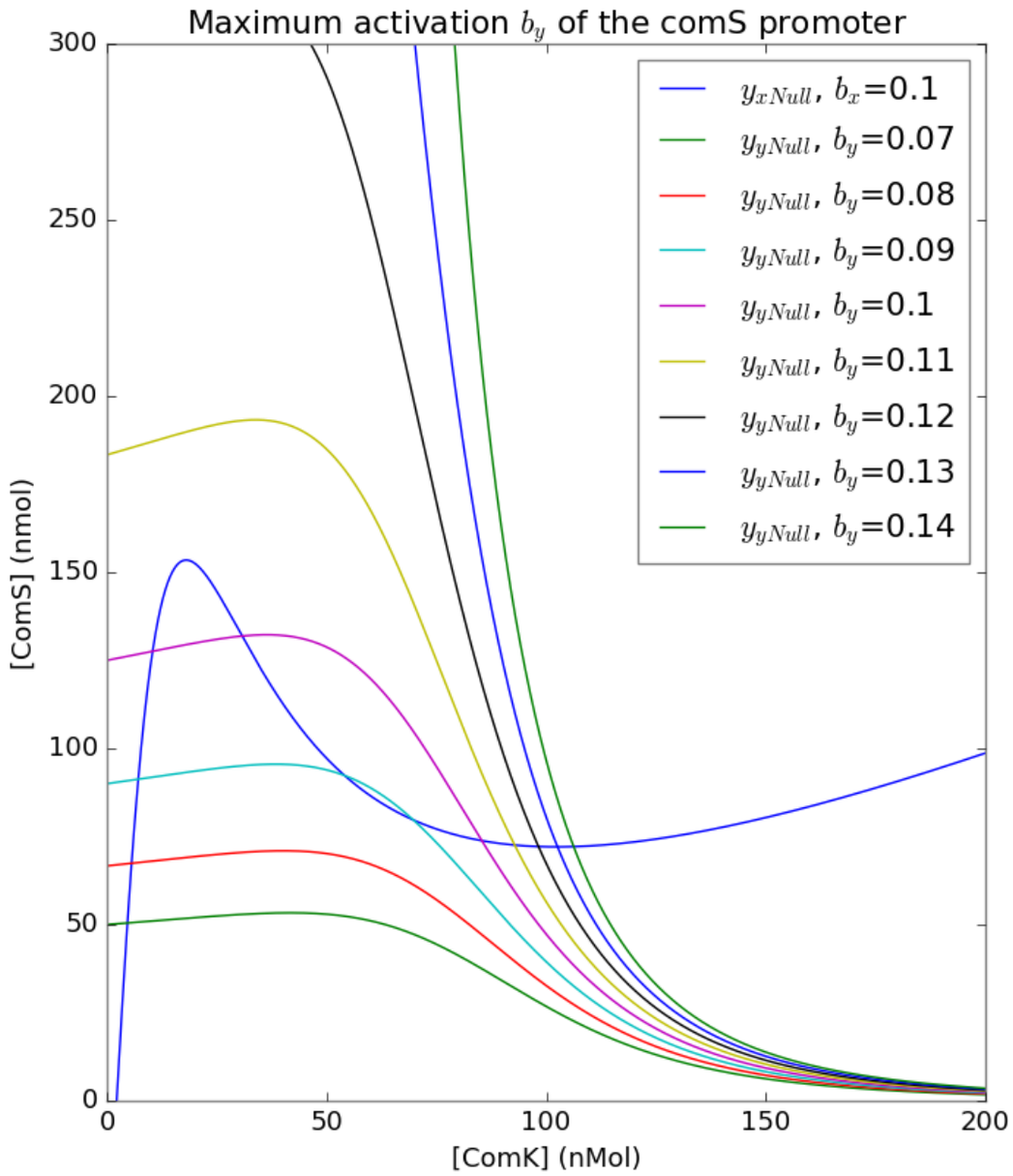
with a function that describes nutrient sensing changes in the rate of activation of the *comS* promoter given by

$$S(n) = \frac{1}{1+\left(\frac{n}{n_0}\right)^2} \tag{3}$$



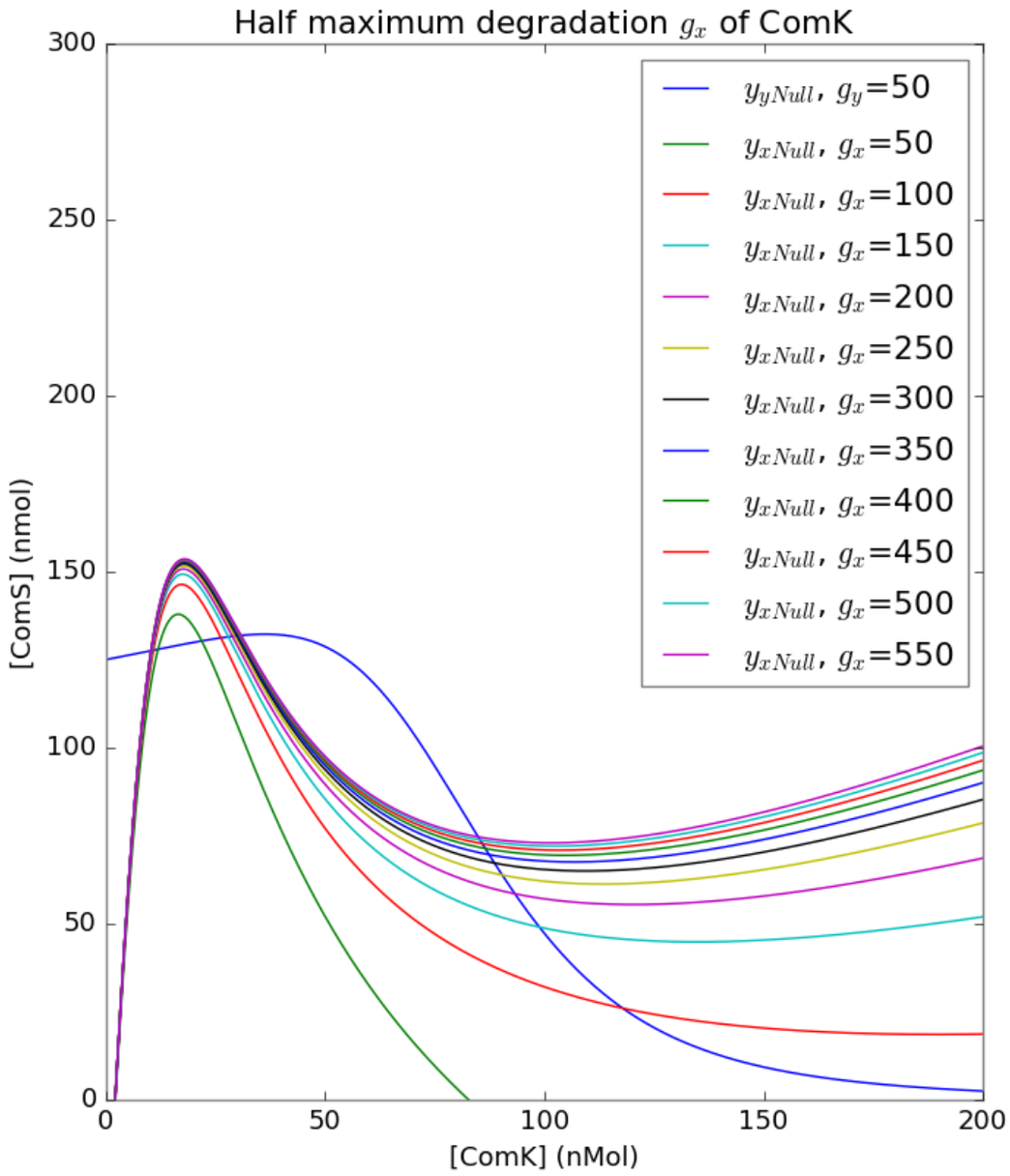
Different roles played by the different parameters that induce *competence*
(Parameters that represent "internal" components that may be noisy)



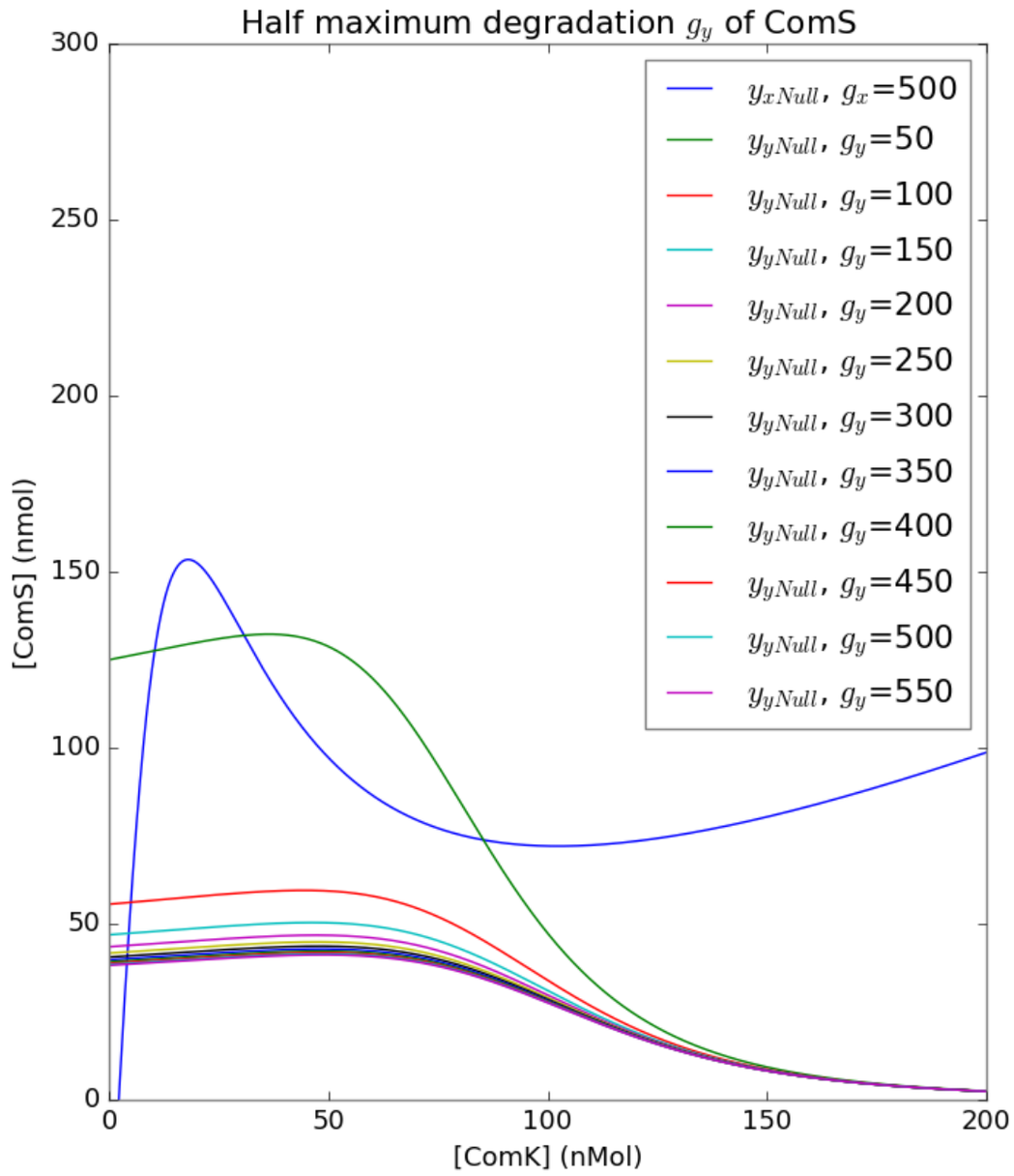


Phase planes obtained by setting different parameter combinations

Increasing the half maximum degradation of ComK enables the possibility of entering into competent states



Increasing the half maximum degradation of ComS induces non-competent steady states



Qualitative changes of different types induced by variations of different parameters