Reliable Behavior or Not?

What is Happening Inside Tiny Organisms?

Drew Endy
Departments of Biological Engineering
MIT → Stanford

ASC @ MIT Media Lab
17 April 2008

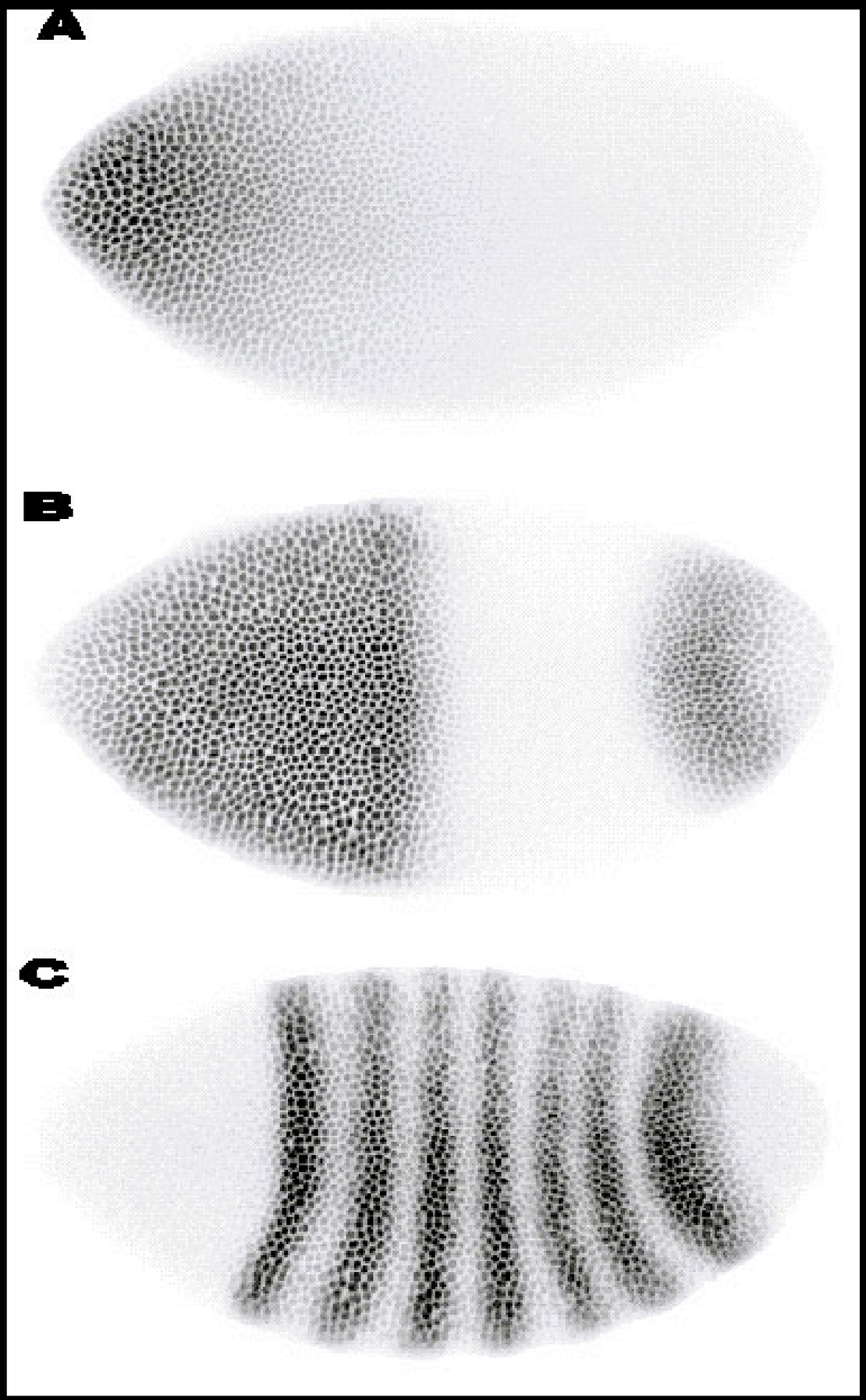
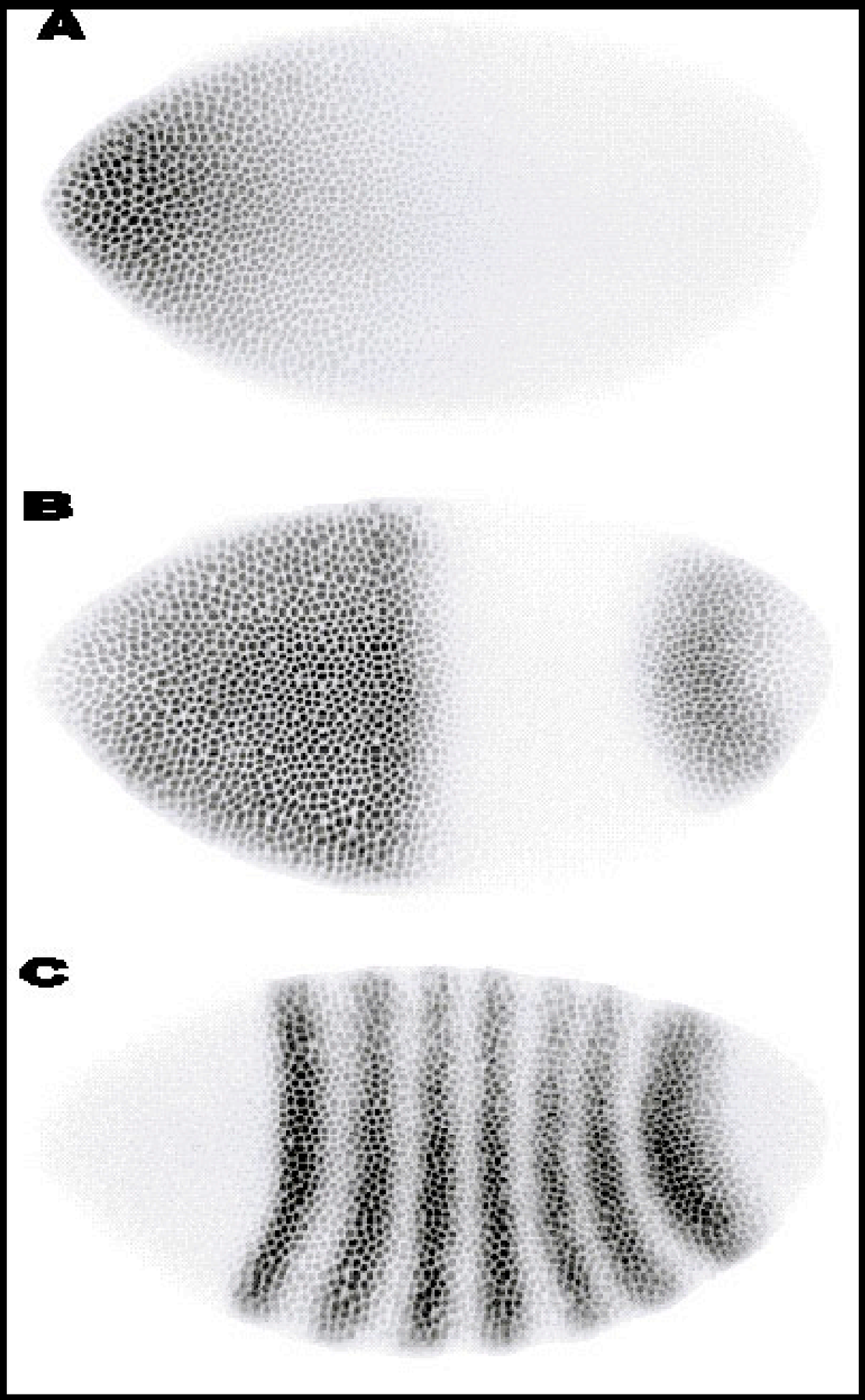


Figure 1: Confocal microscope images of a fruit fly embryo, stained with fluorescent antibodies to three different gene products (Bicoid, Hunchback and Even-skipped)

http://www.bioinfo.de/isb/2003/03/0009/main.html



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Establishment of developmental precision and proportions in the early *Drosophila* embryo

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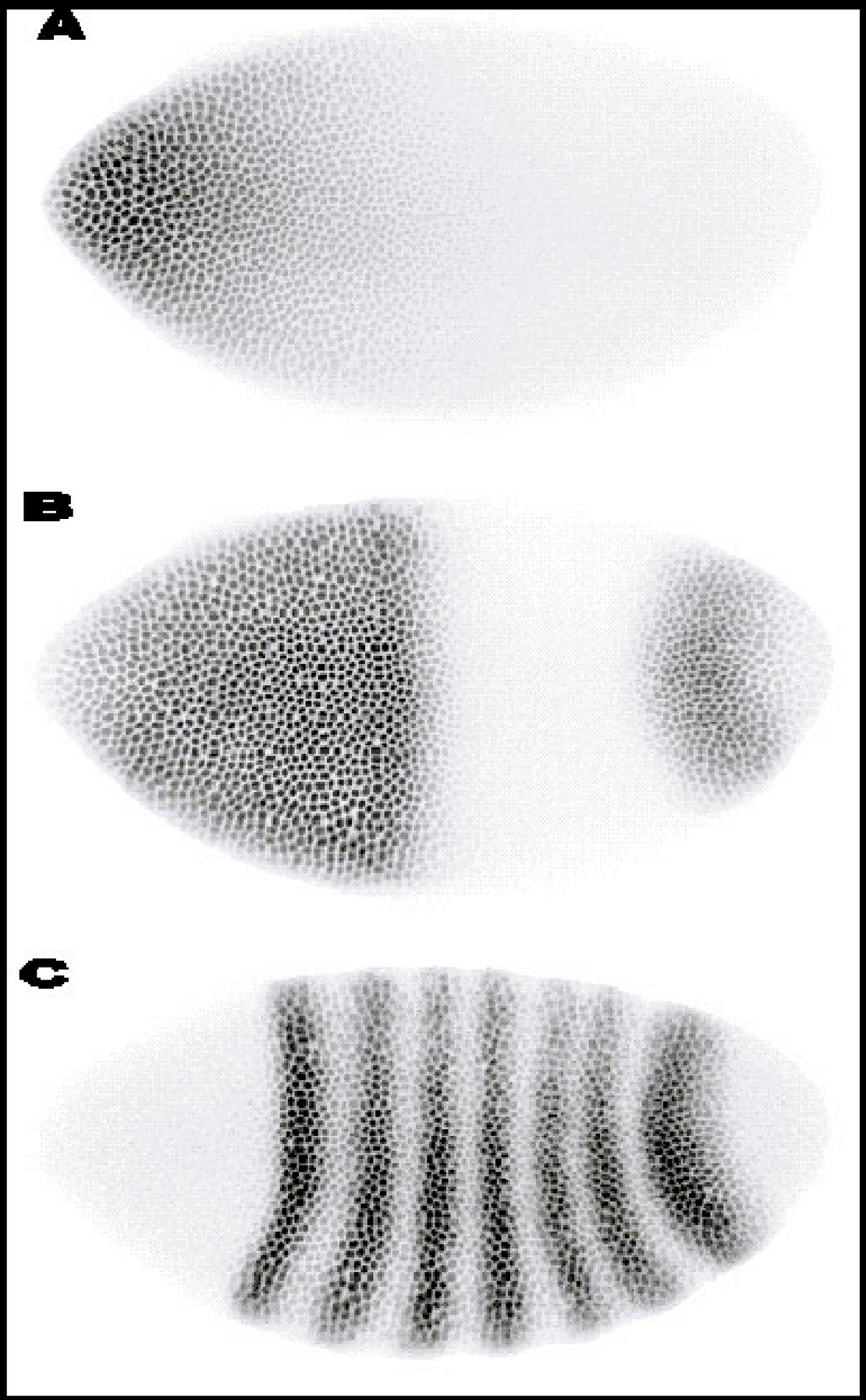
During embryonic development, orderly patterns of gene expression eventually assign each cell in the embryo its particular fate. For the anteroposterior axis of the *Drosophila* embryo, the first step in this process depends on a spatial gradient of the maternal morphogen Bicoid (Bcd). Positional information of this gradient is transmitted to downstream gap genes, each occupying a well defined spatial domain[1–4]. We determined the precision of the initial process by comparing expression domains in different embryos. Here we show that the Bcd gradient displays a high embryo-to-embryo variability, but that this noise in the positional information is strongly decreased ('filtered') at the level of *hunchback* (*hb*) gene expression. In contrast to the Bcd gradient, the *hb* expression pattern already includes the information about the scale of the embryo. We show that genes known to interact directly with Hb are not responsible for its spatial precision, but that the maternal gene *staufen* may be crucial.



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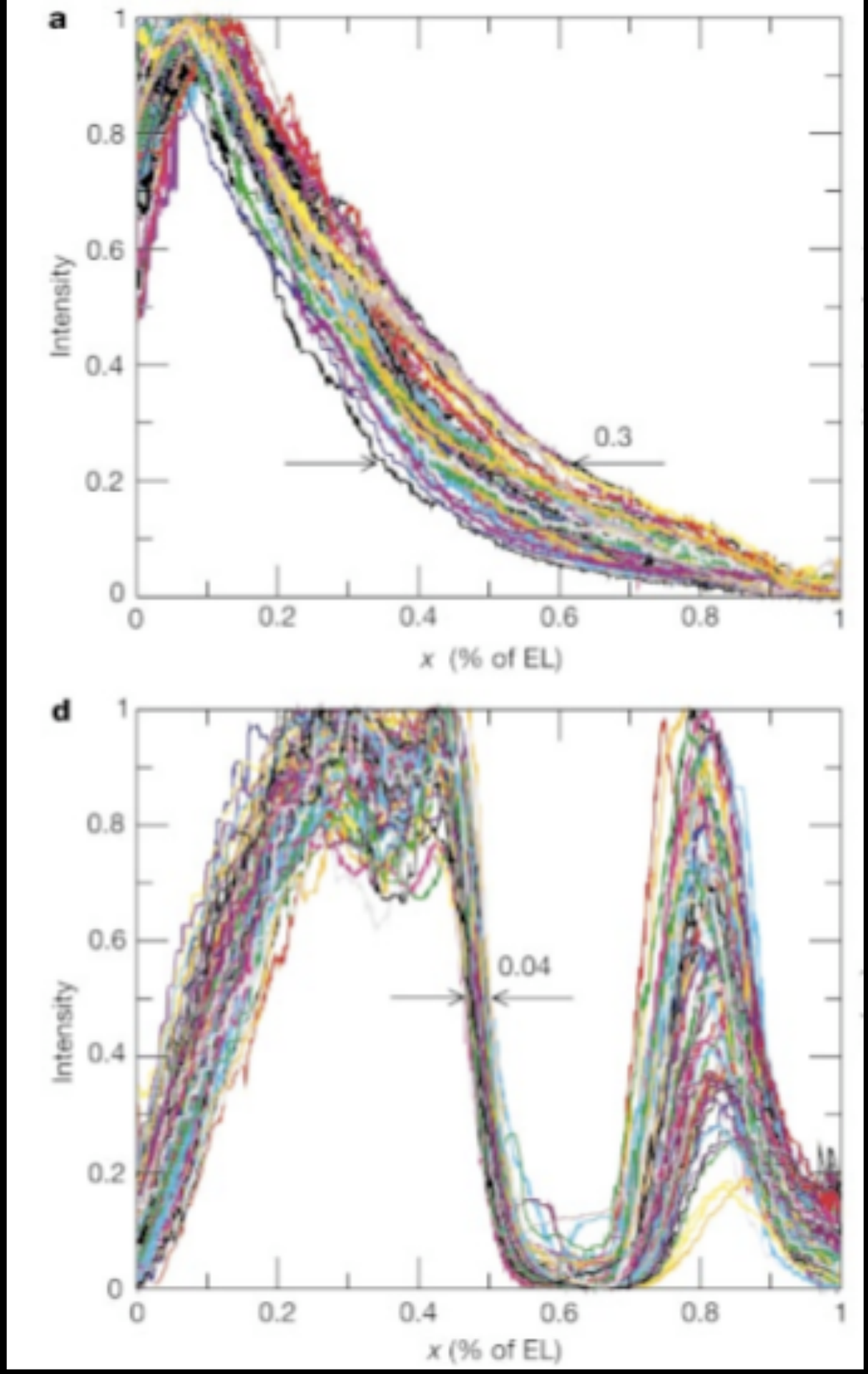

Stochastic Kinetic Analysis of Developmental Pathway Bifurcation in Phage λ-Infected *Escherichia coli* Cells

Adam Arkin,*[,1] John Ross[†] and Harley H. McAdams*

**Department of Developmental Biology and [†]Department of Chemistry, Stanford University, Stanford, California 94305*

Manuscript received March 5, 1998
Accepted for publication April 30, 1998

ABSTRACT

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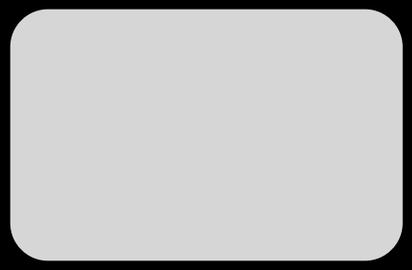

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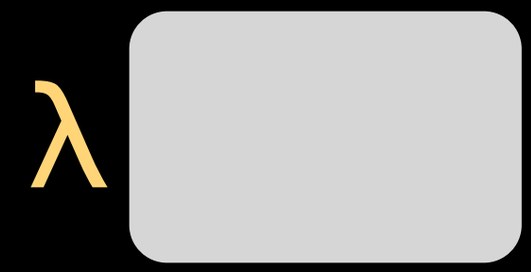

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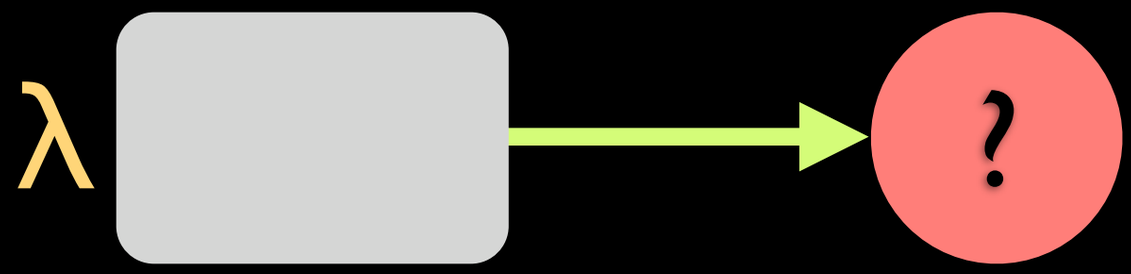

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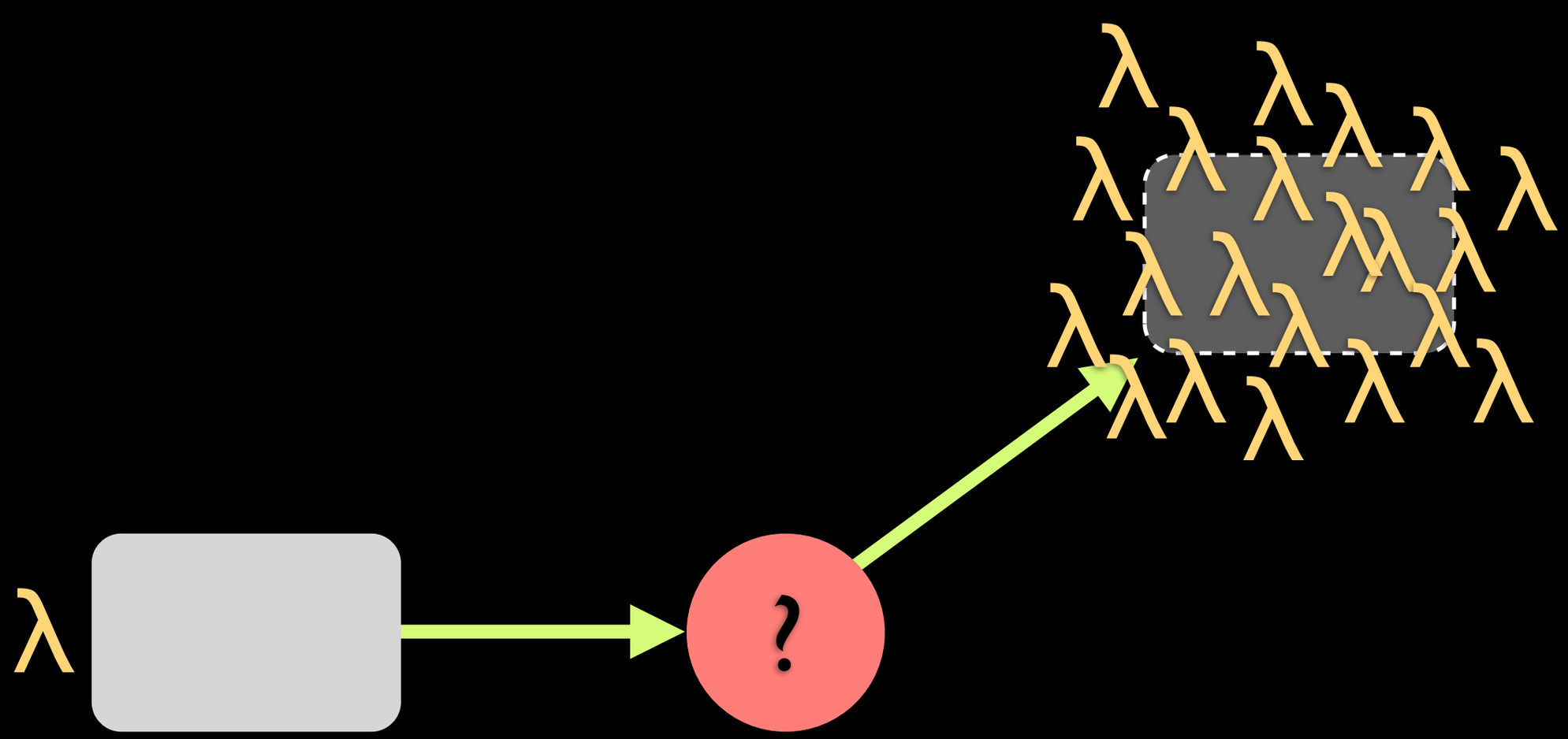

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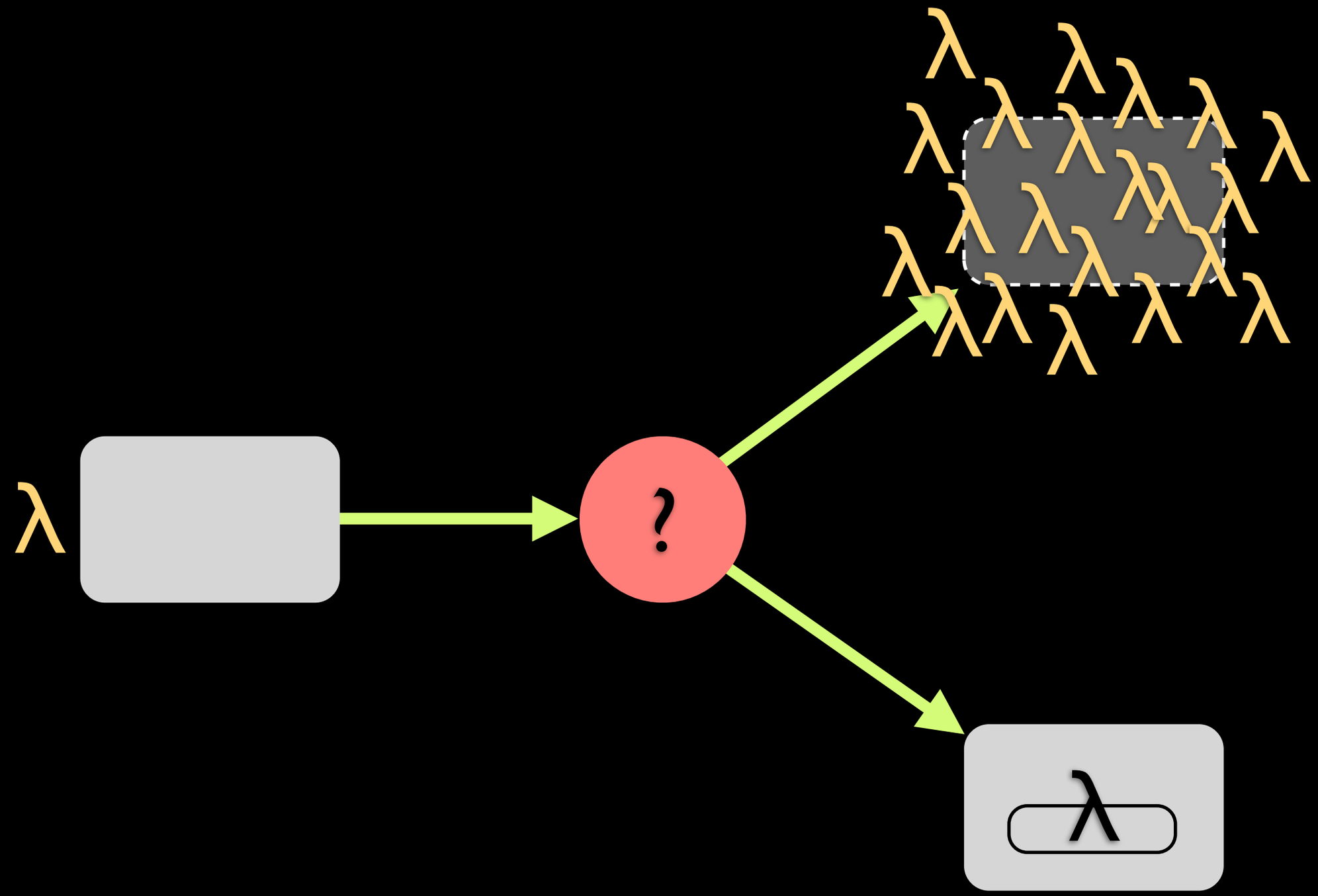

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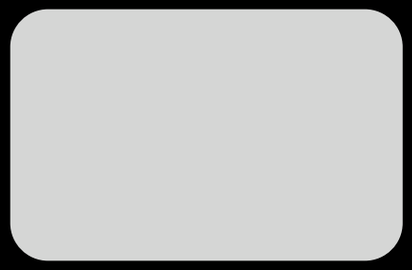

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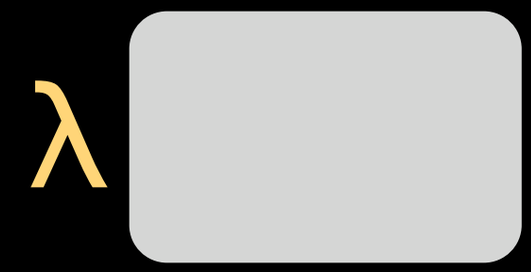

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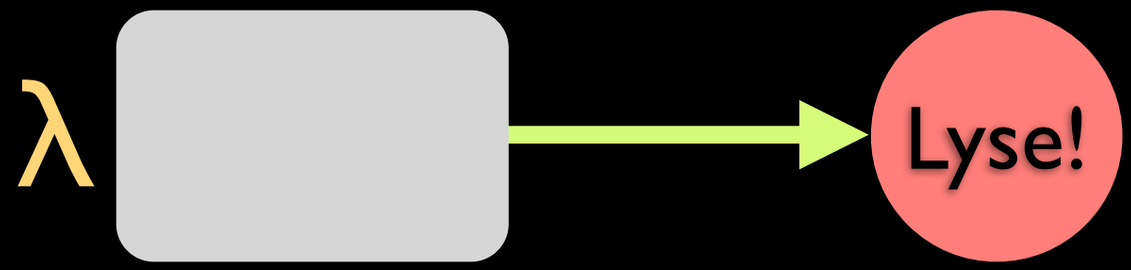

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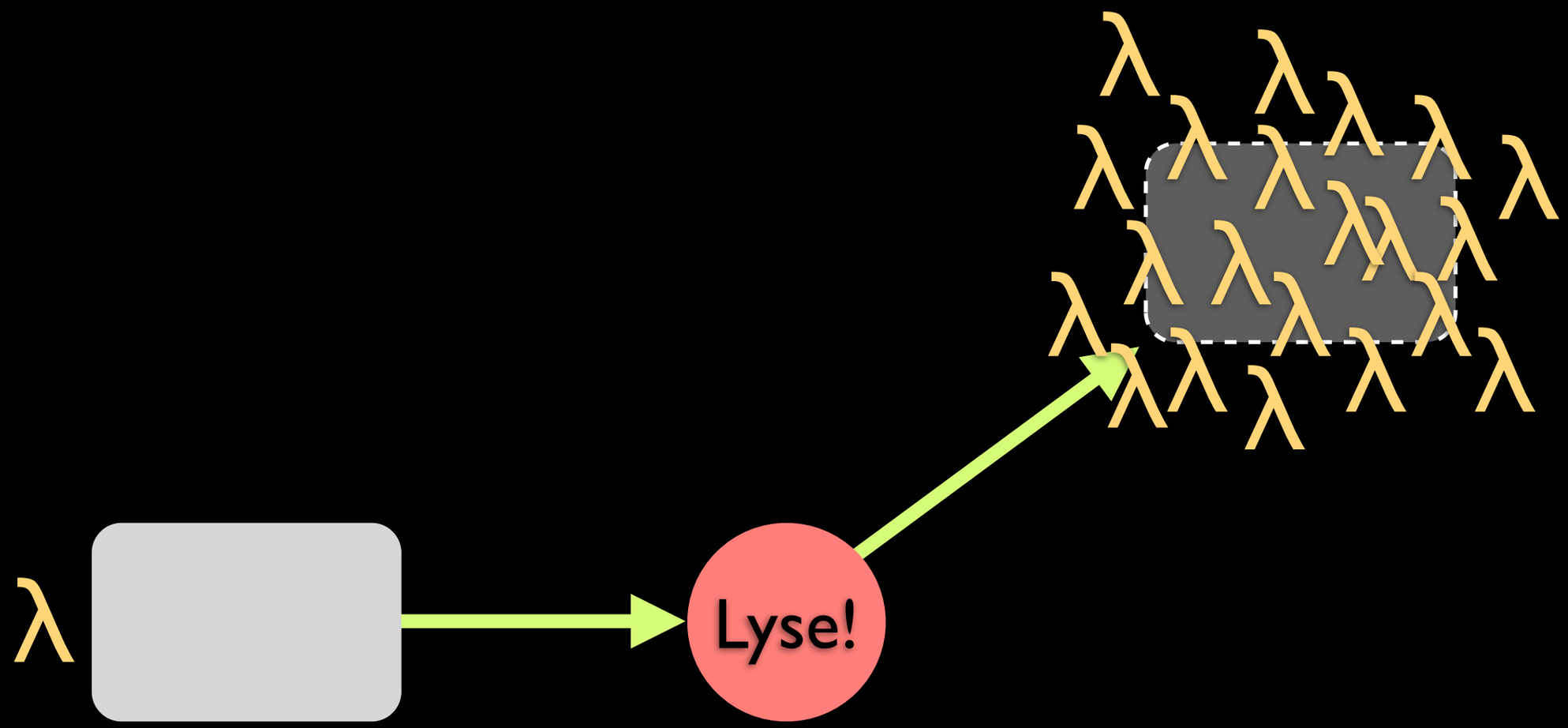

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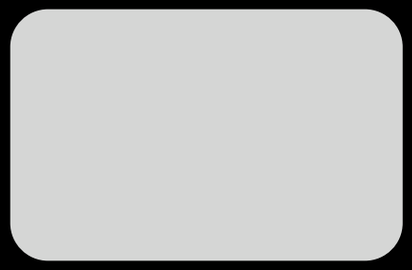

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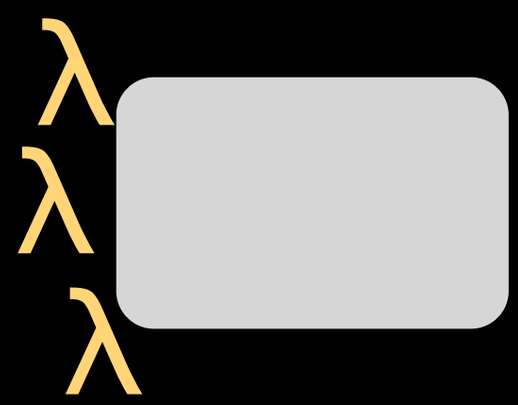

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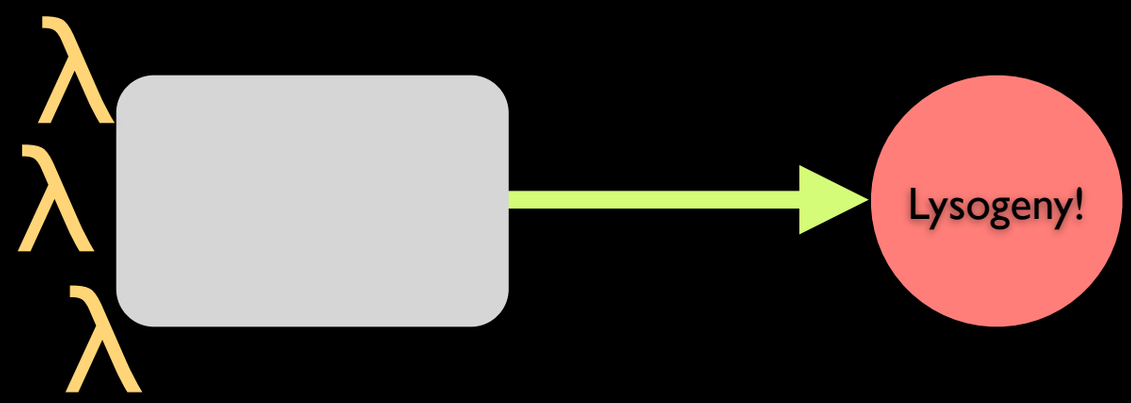

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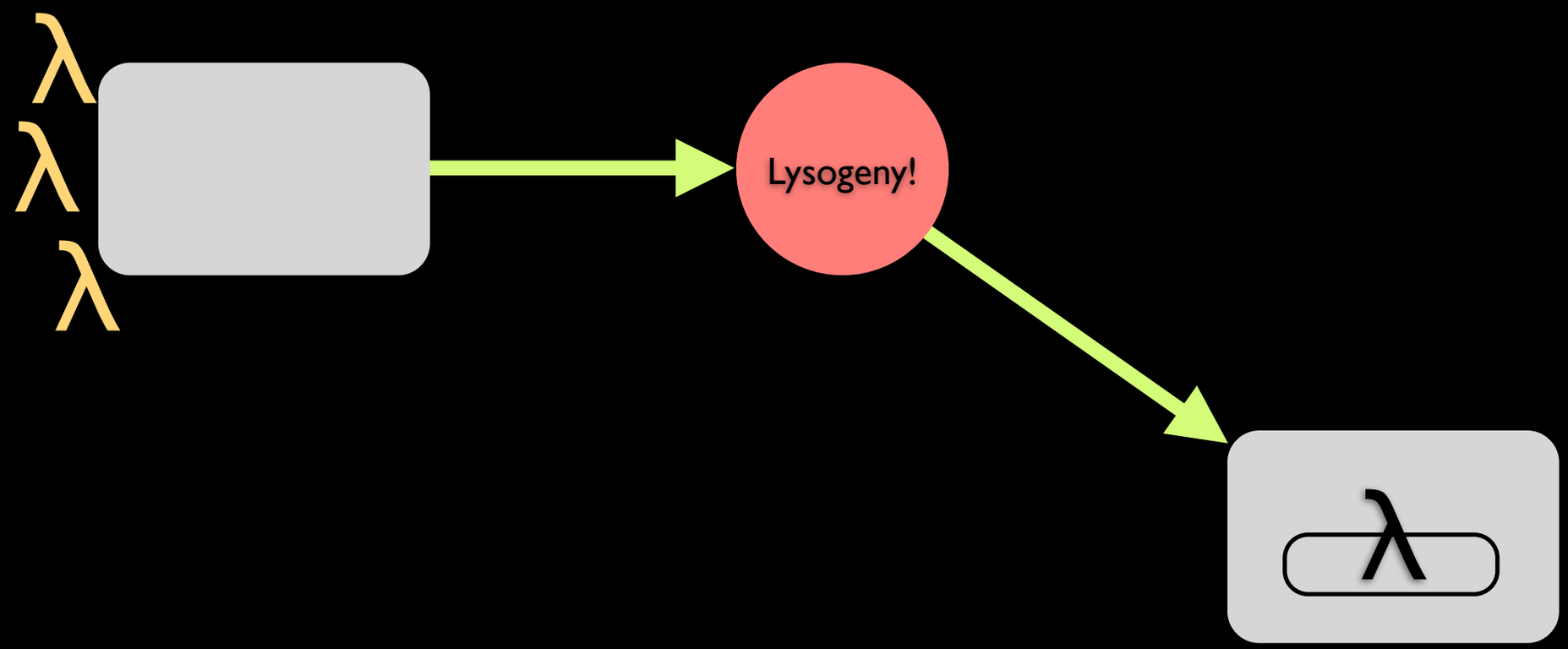

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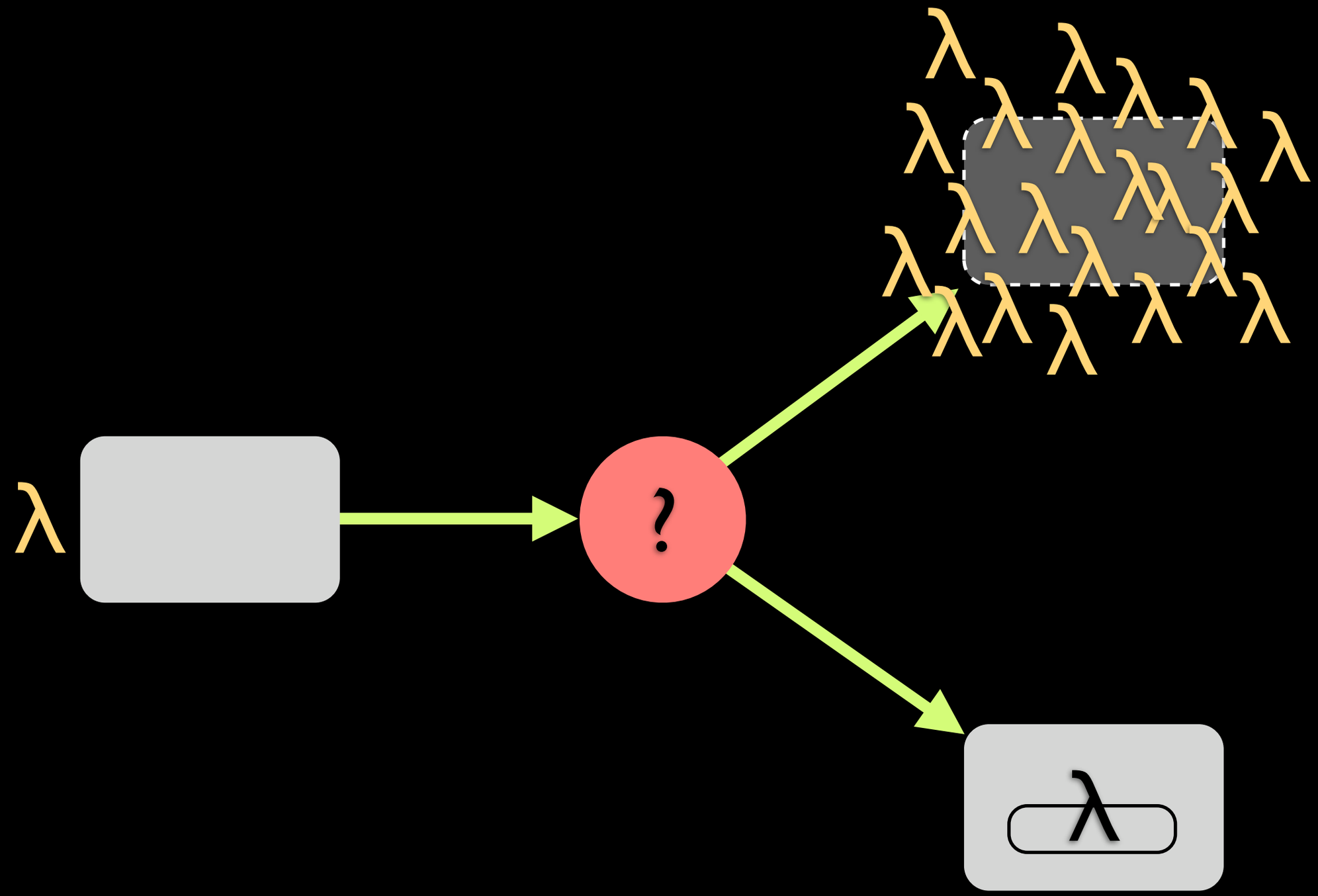

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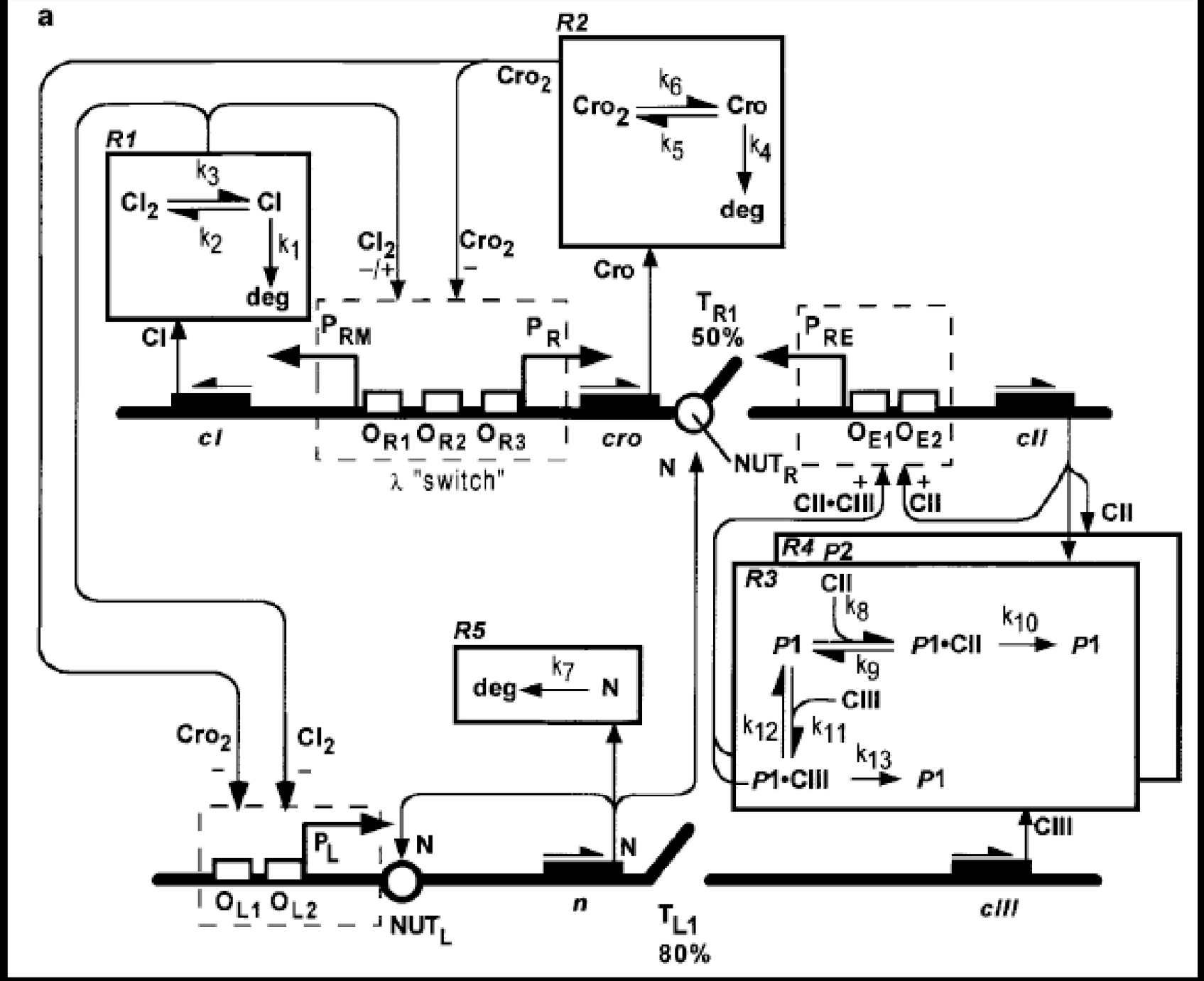

Arkin, Ross & McAdams
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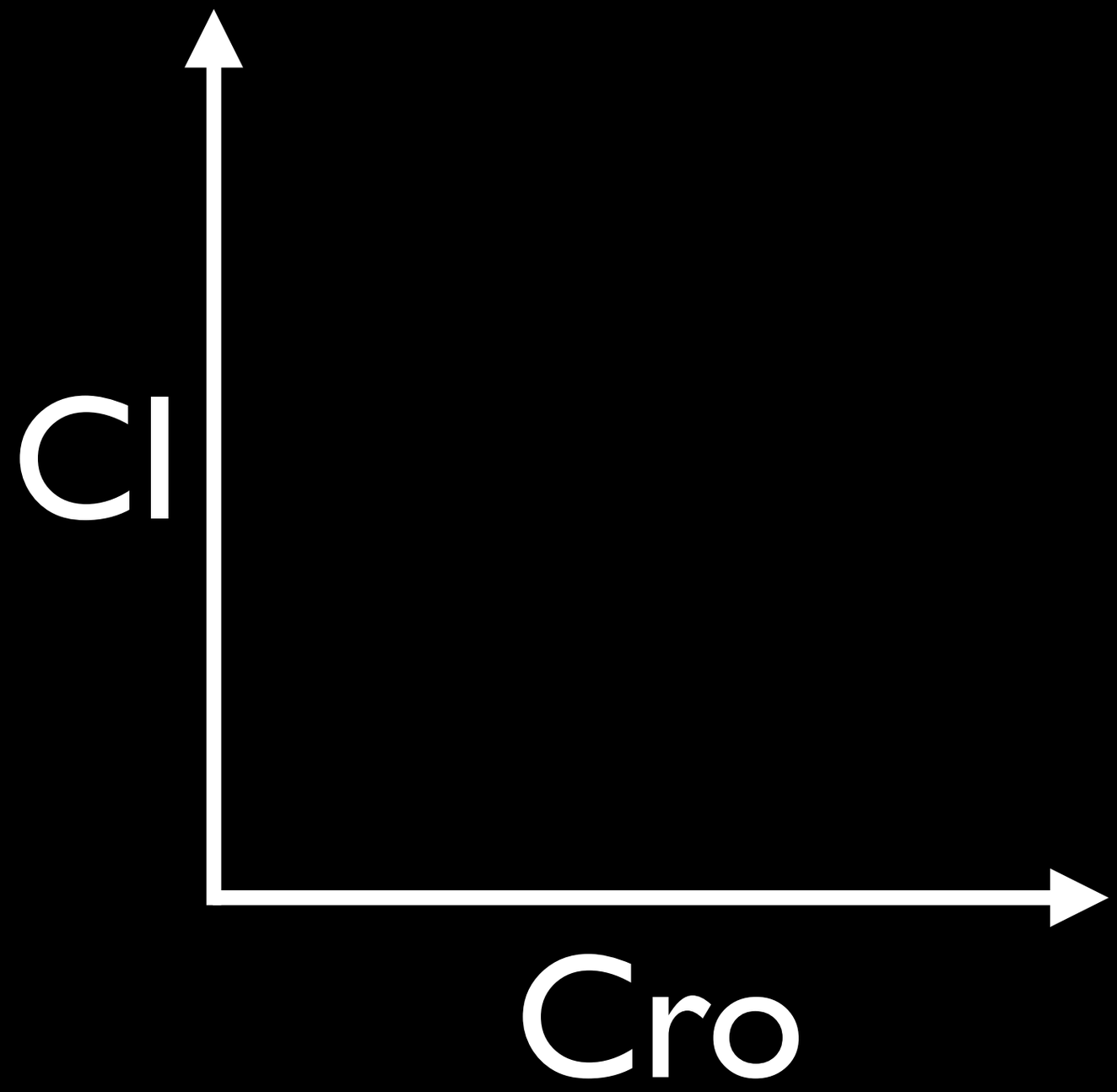
Genetics 149:1633 (1998)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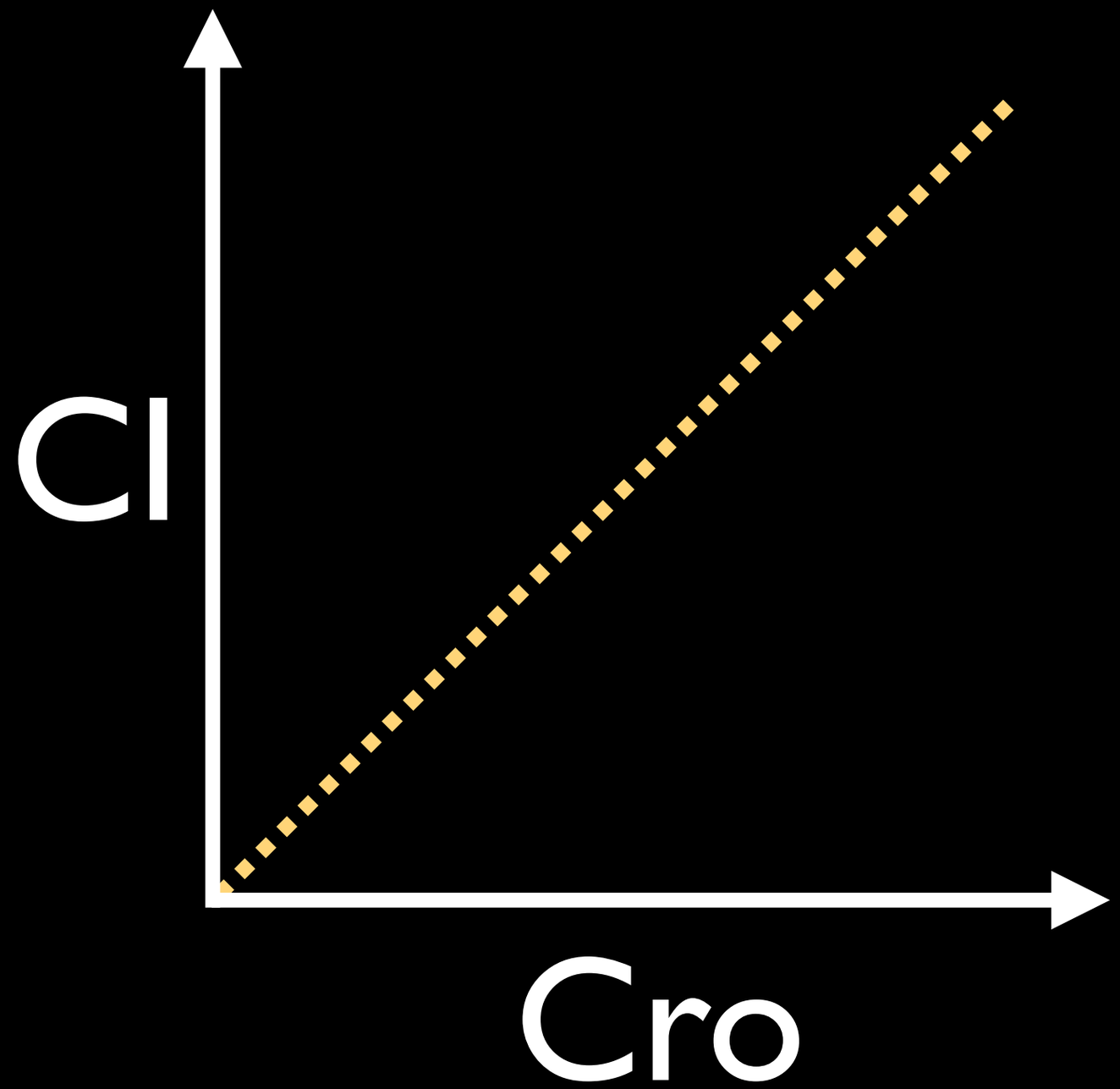
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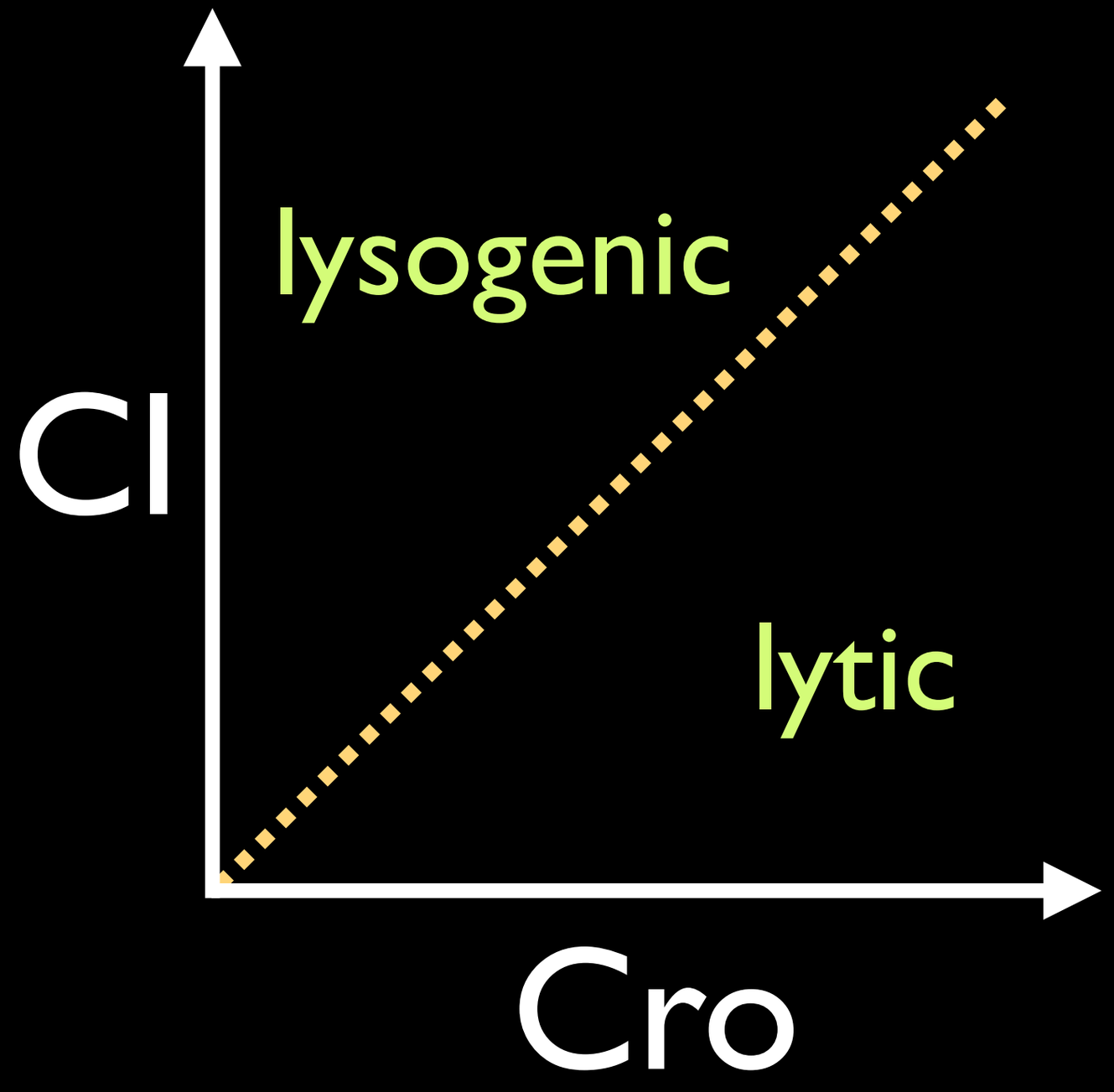
lysogenic
CI
lytic
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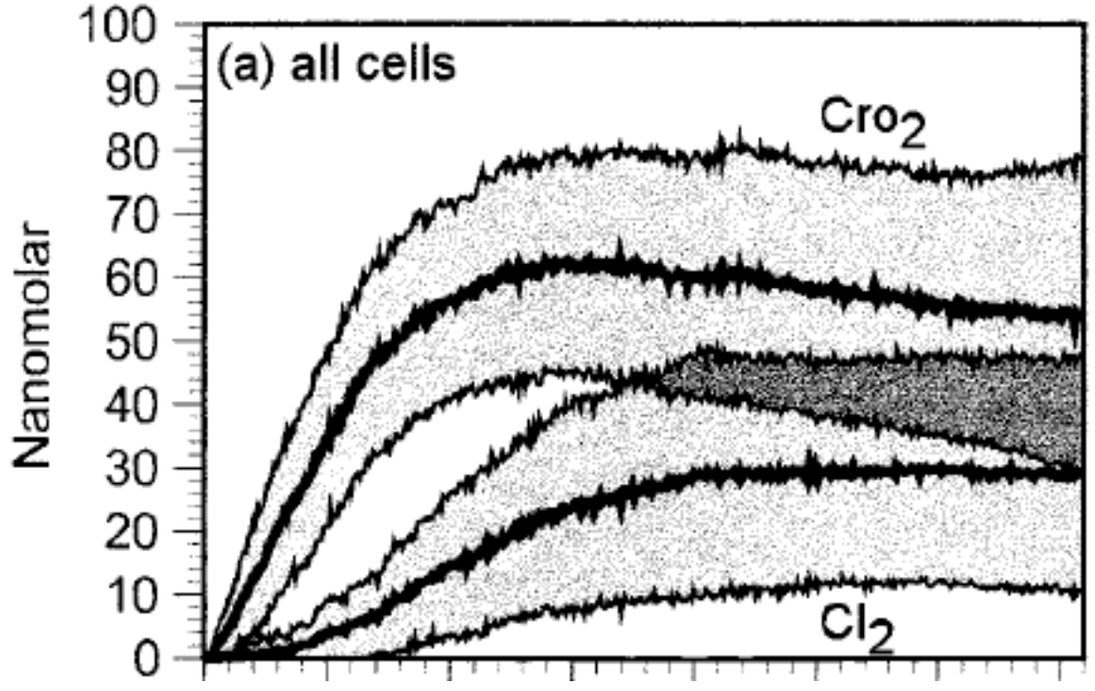

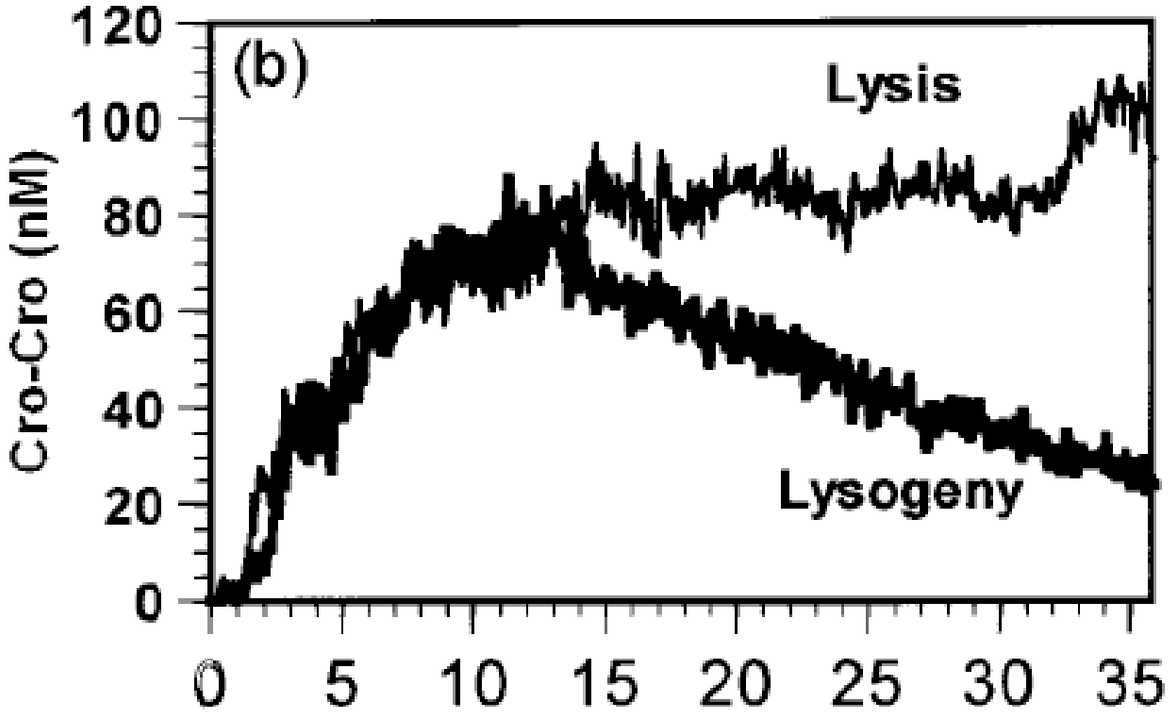

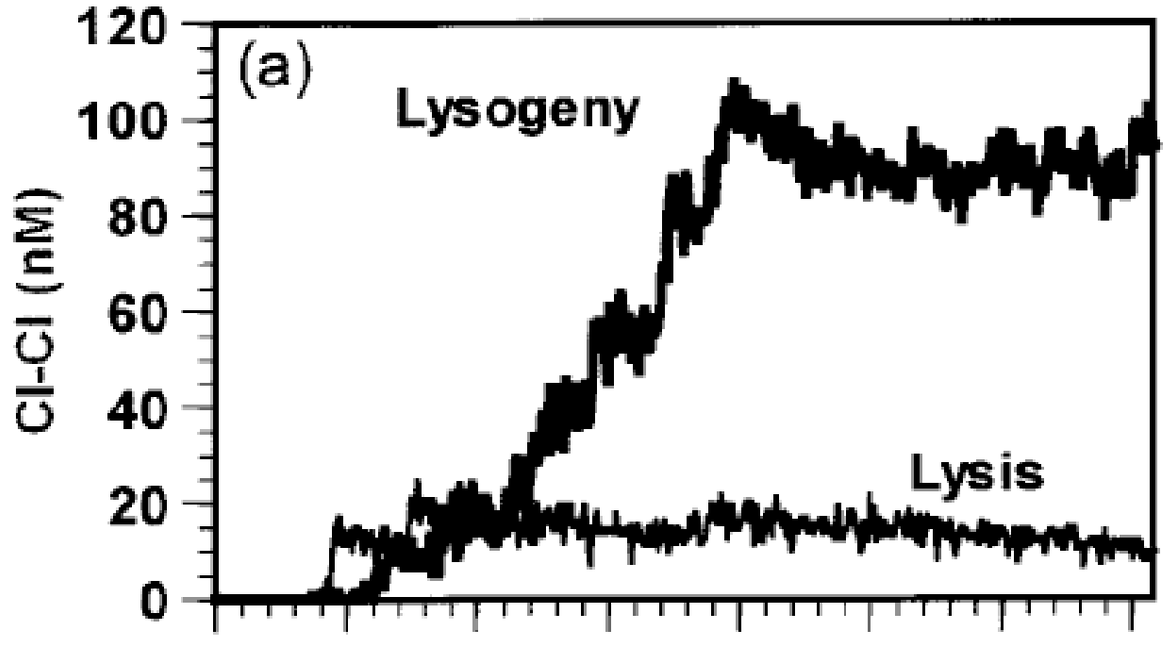

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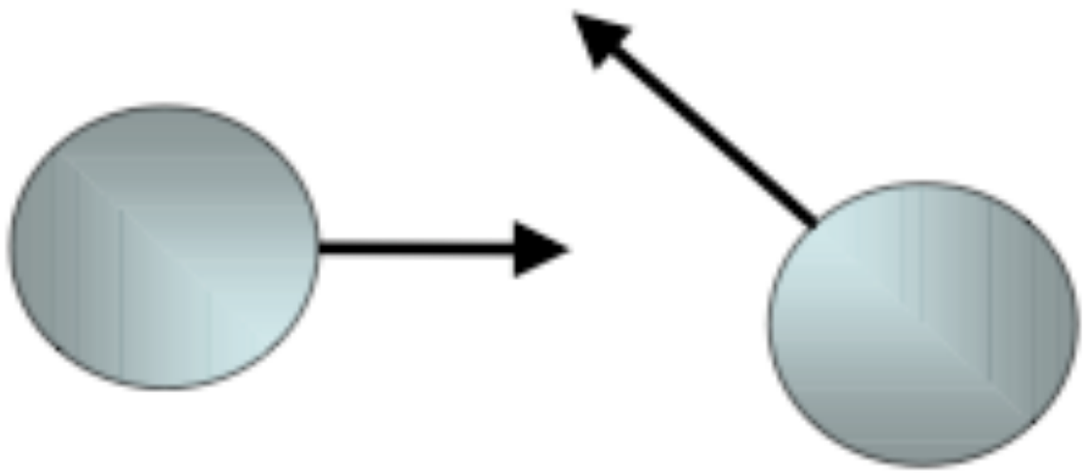
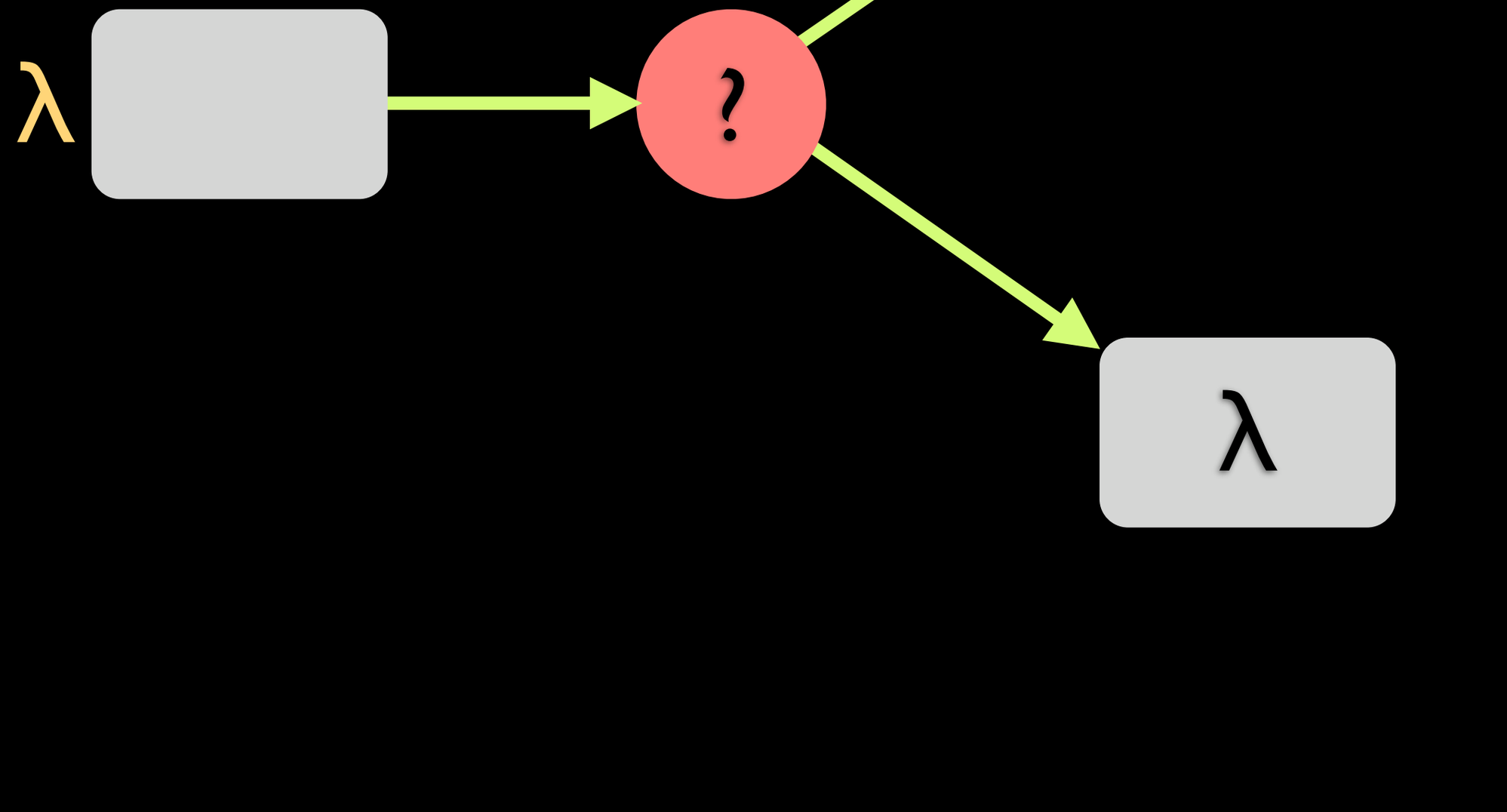
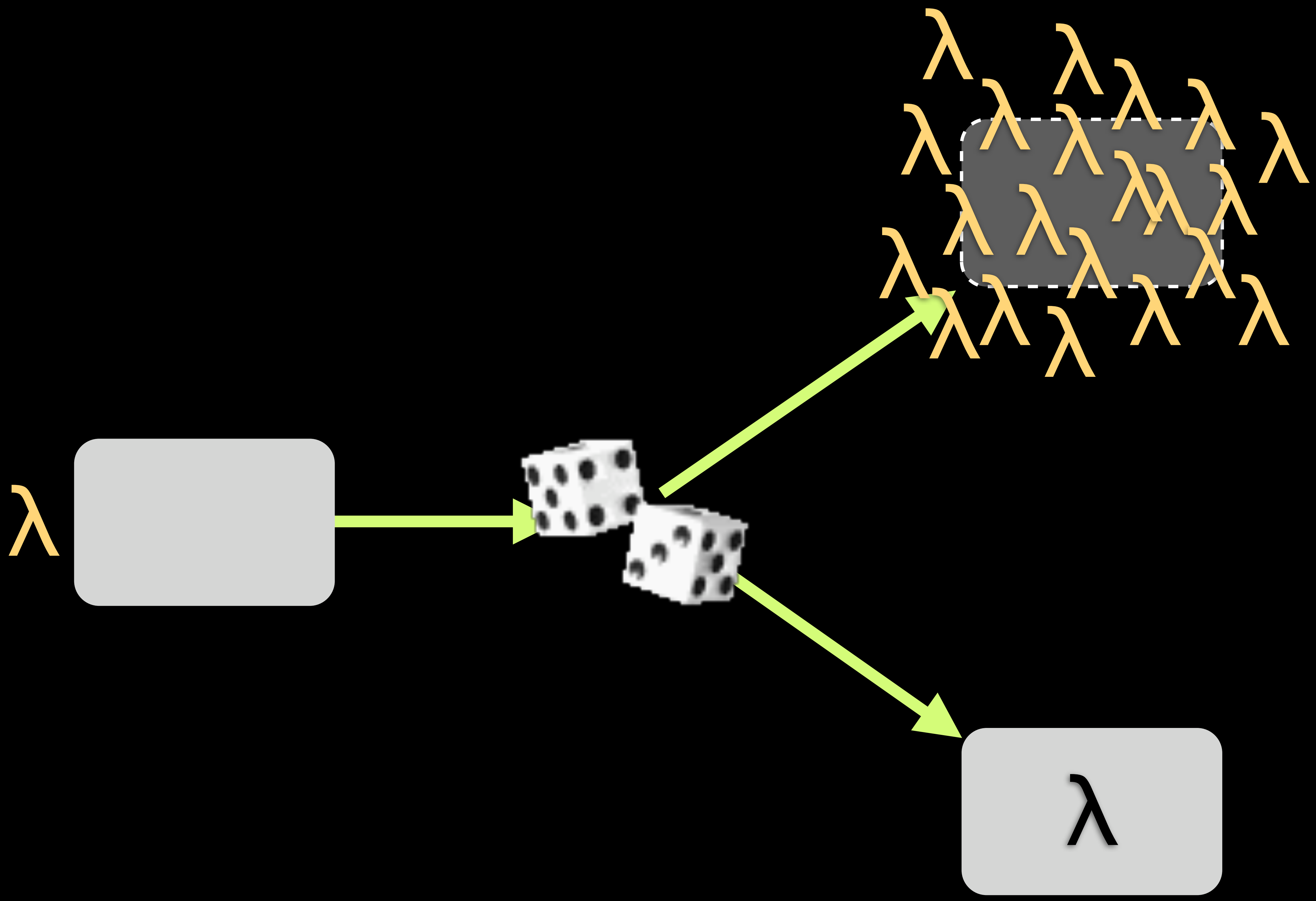
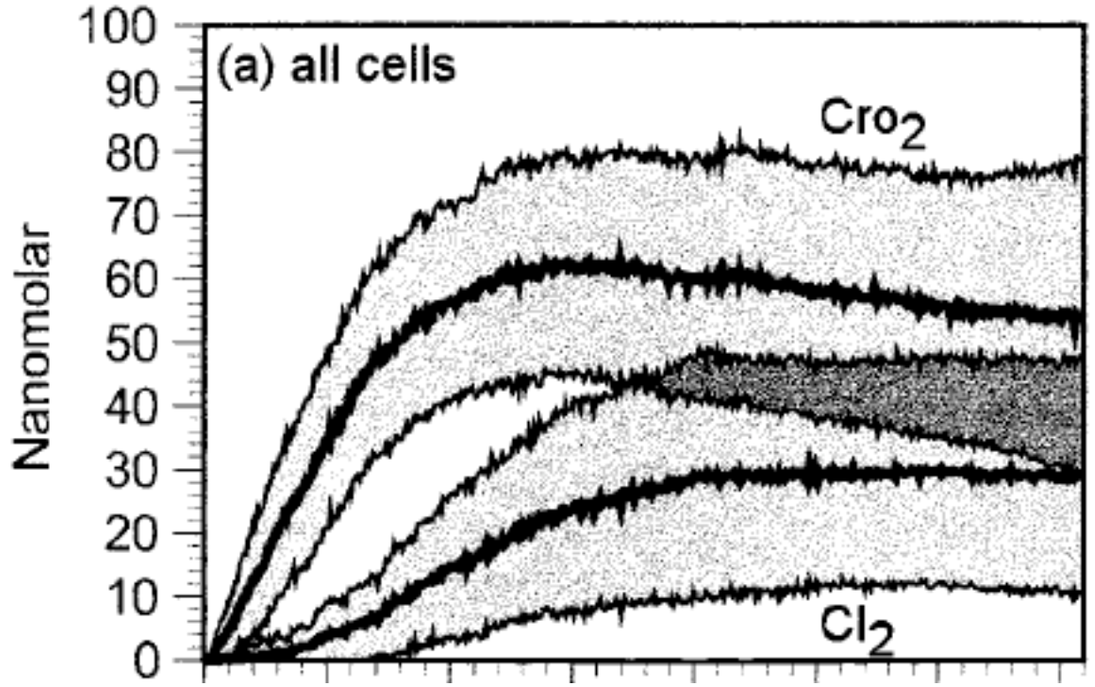


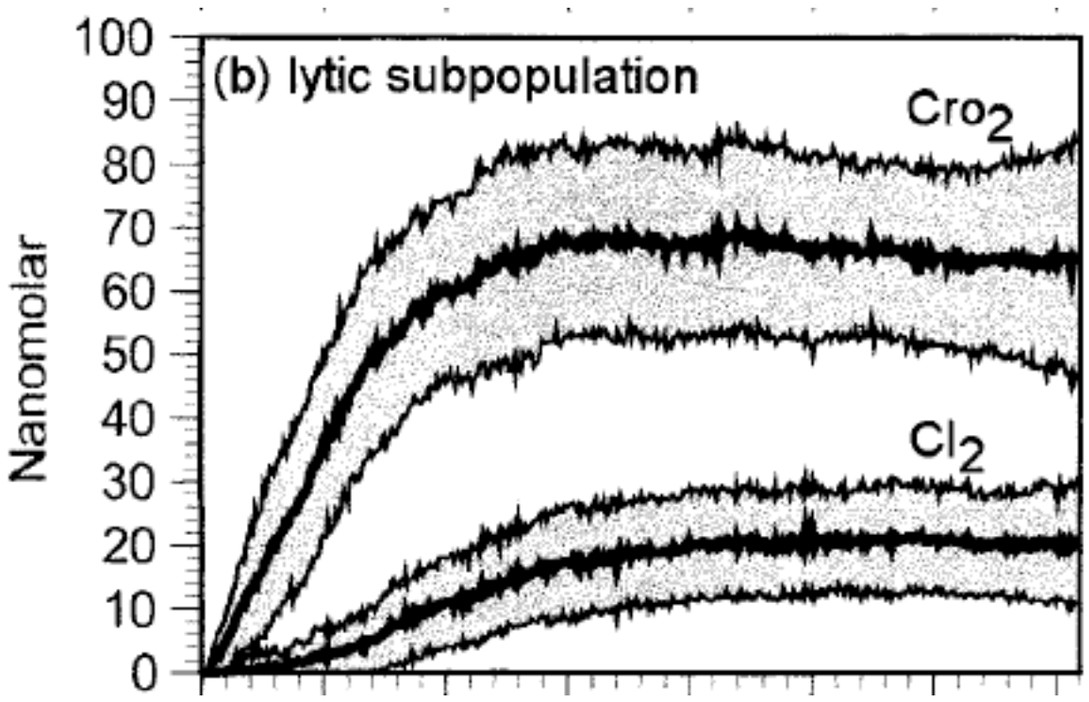
$$c_\upsilon \delta t = V^{-1} \pi d_{12}^{\,2} (8kT/\pi m_{12})^{0.5} e^{(-\mu_\upsilon/kT)} \delta t$$

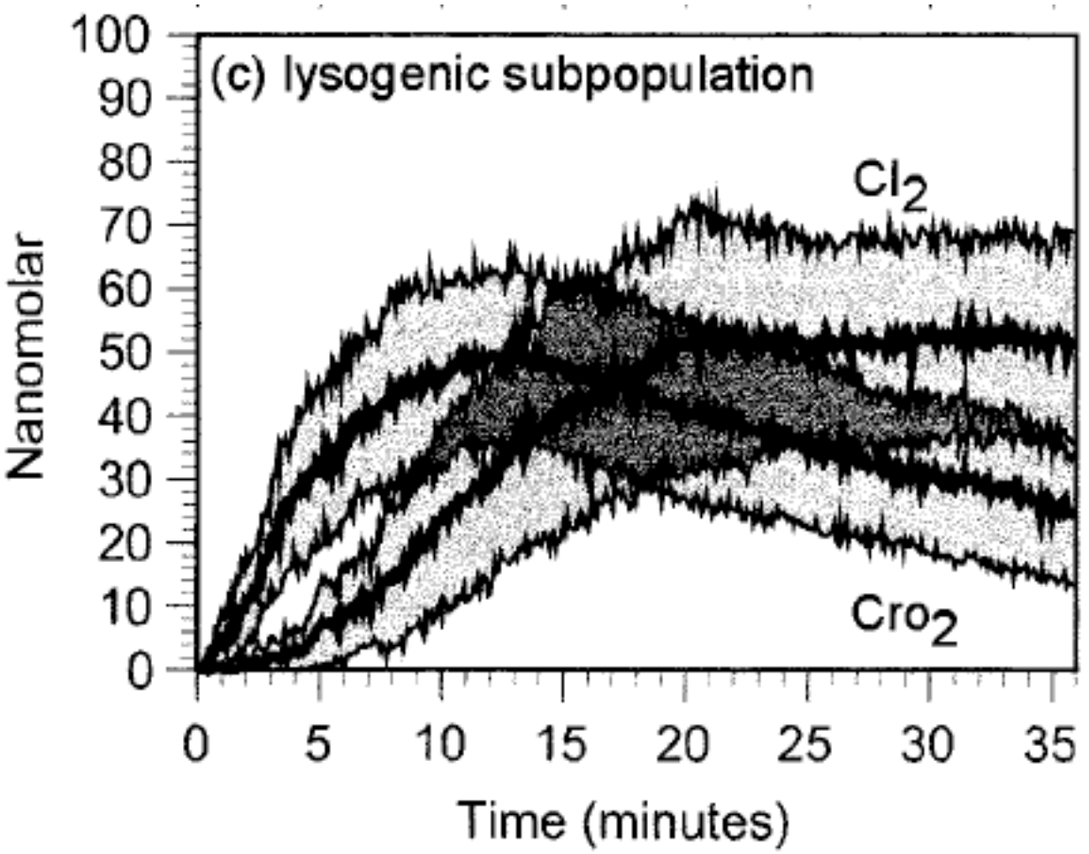
Daniel T. Gillespie, Journal of Computational Physics v22 p403-434, 1976


λ
?
λ


λ







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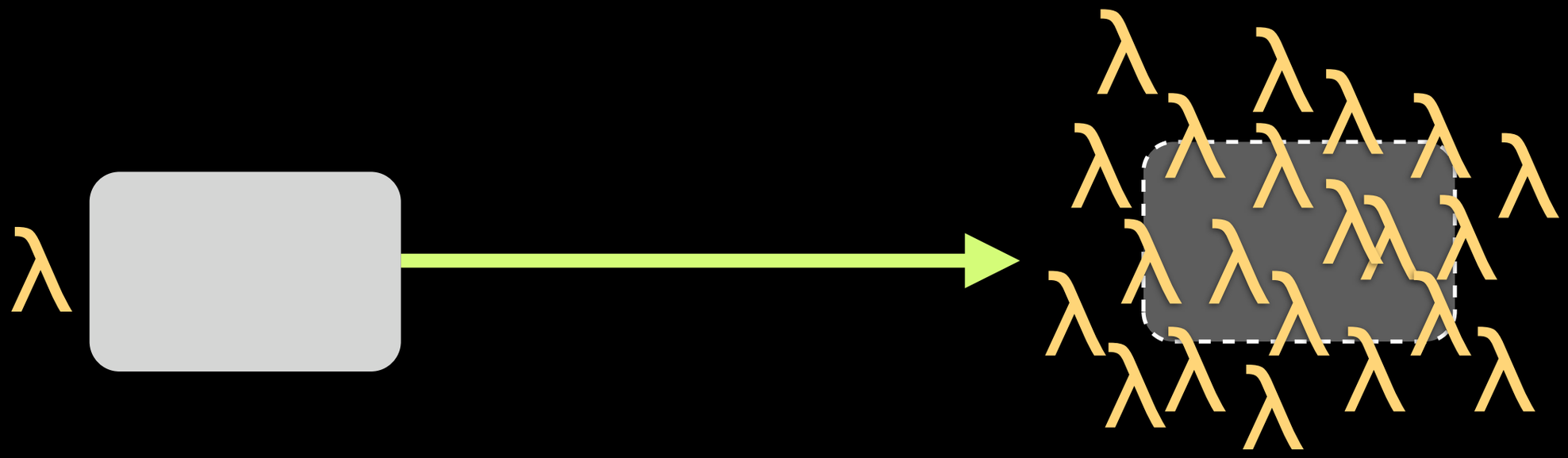
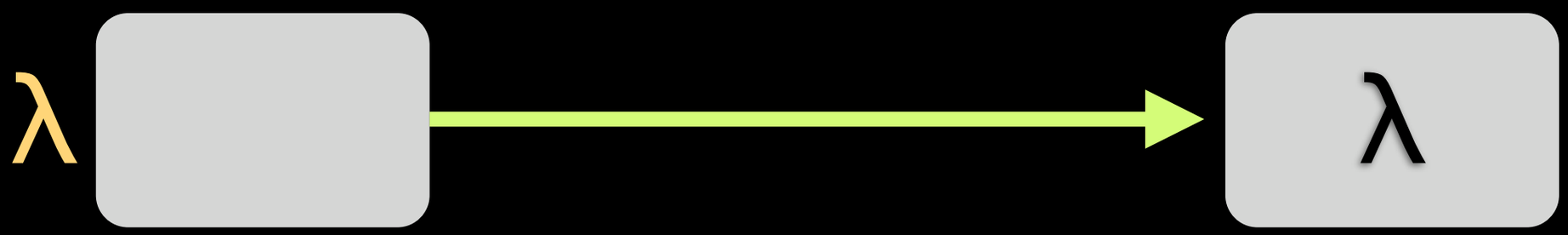
λ

λ λ λ





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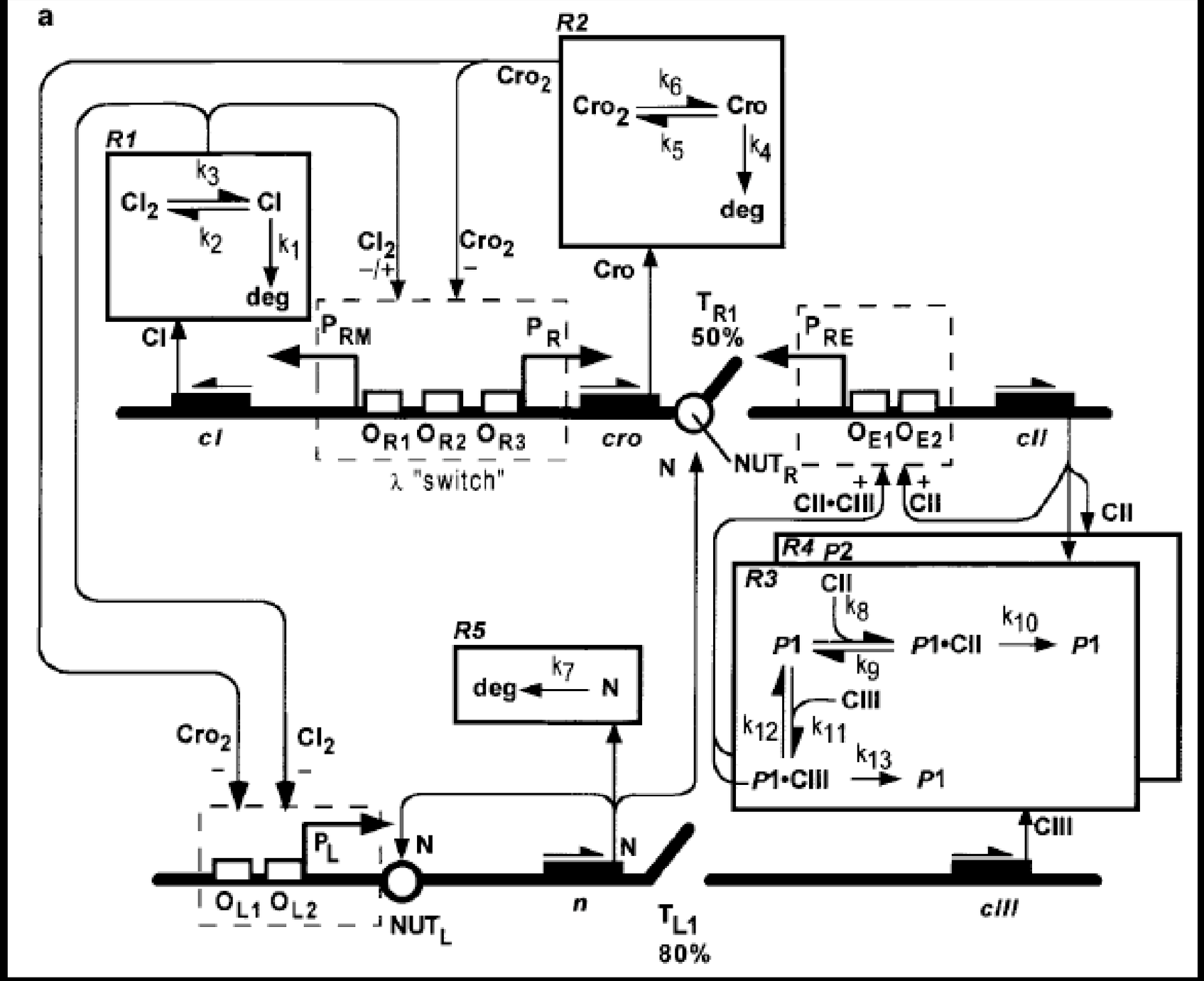

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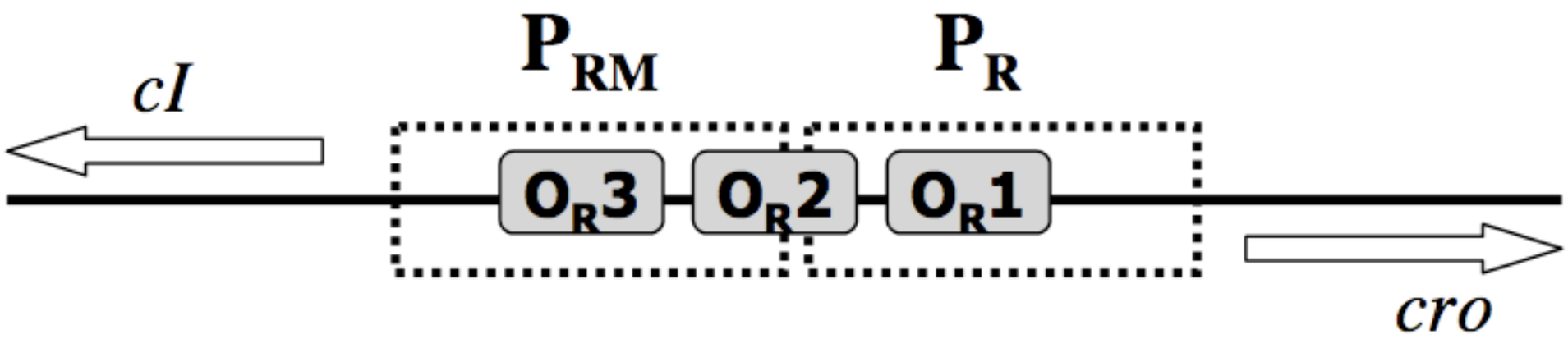
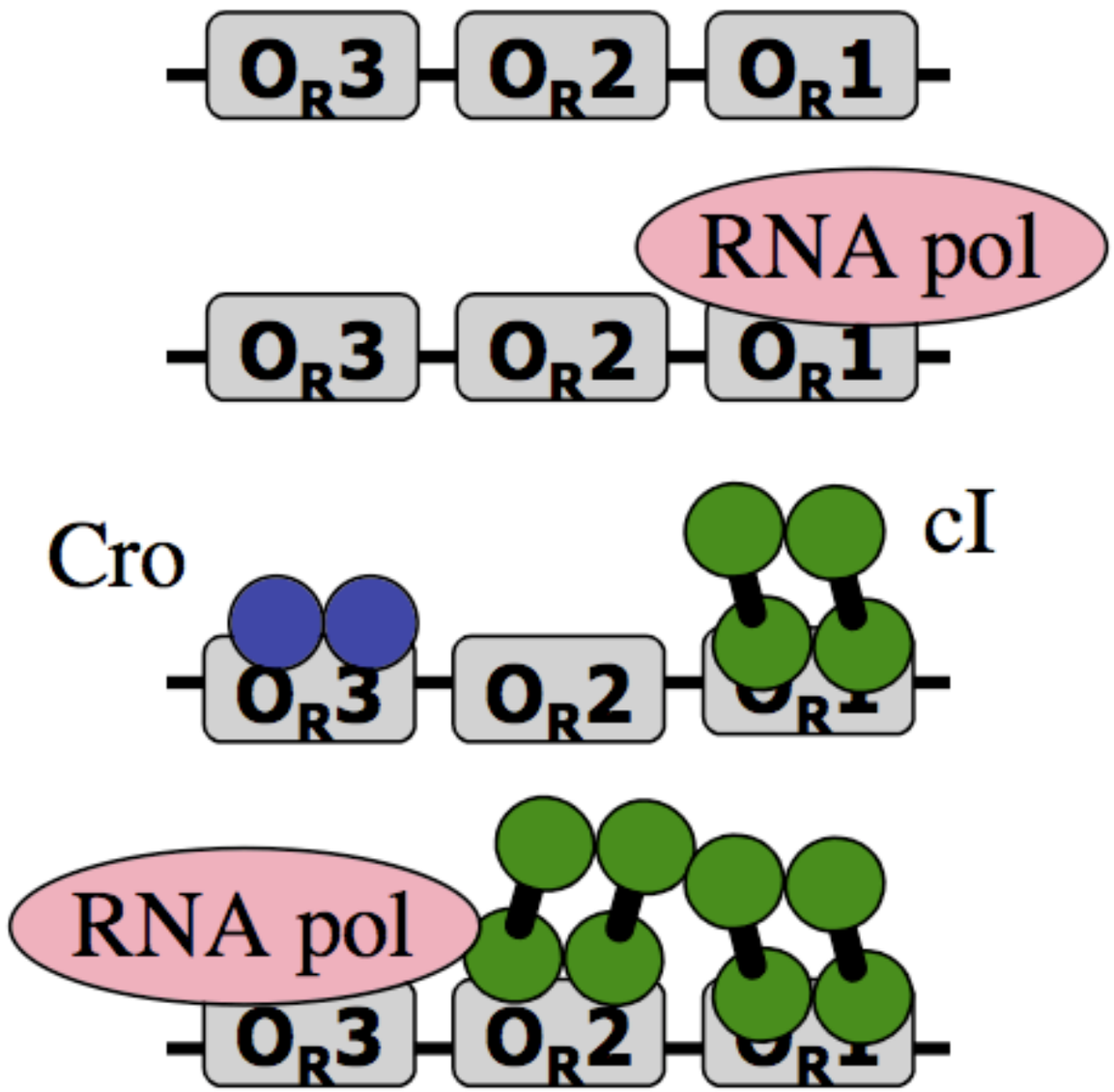

P_RM
P_R
cI
O_R3
O_R2
O_R1
cro

Shea & Ackers care of:
Reinitz J, Vaisnys JR.
J Theor Biol. 145(3):295-318 (1990).

TABLE 3

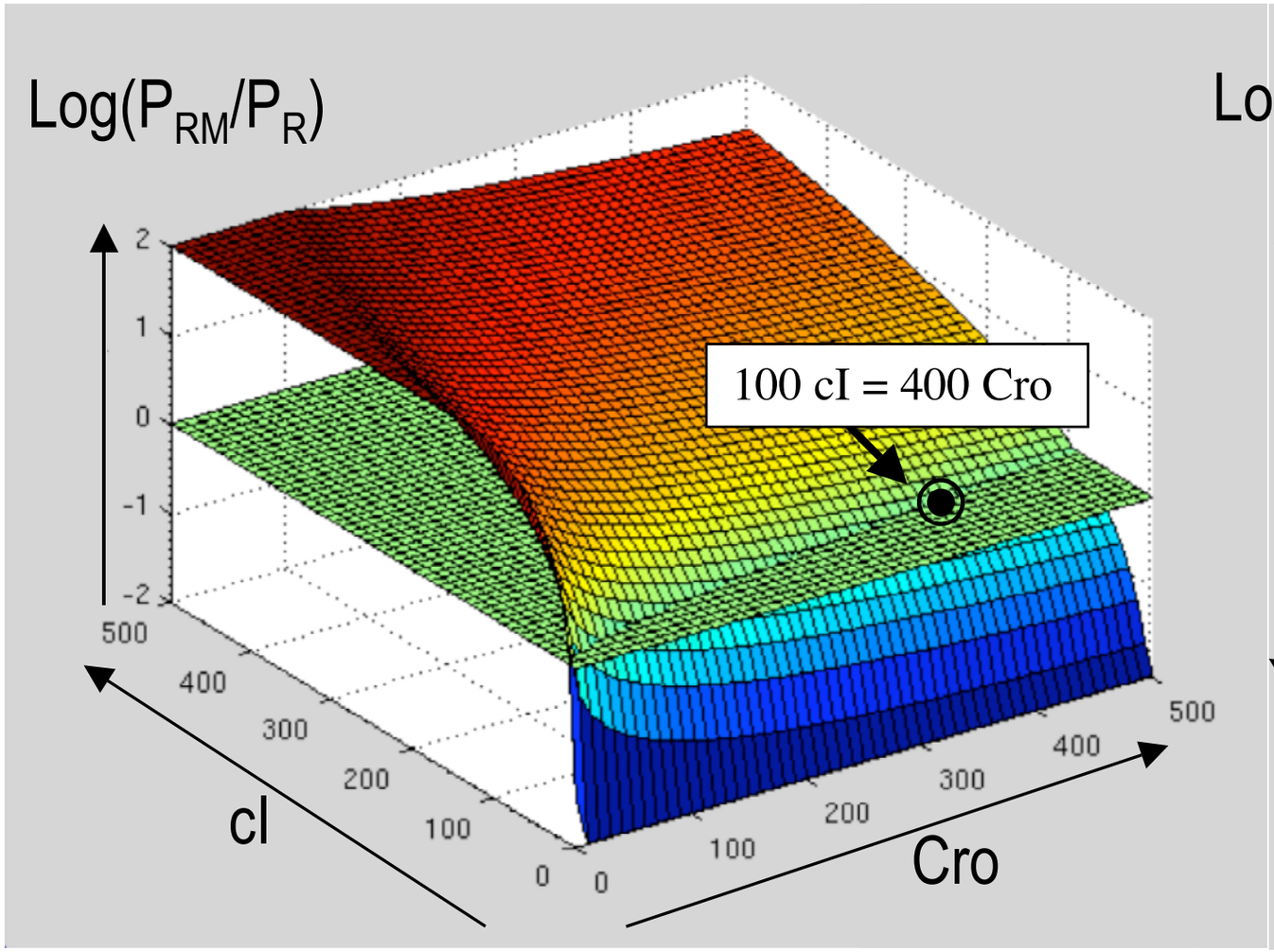
Binding states of O_R

State	P_{RM}	O_R3	O_R2	O_R1	P_R	ΔG_s (kcal mol^{-1})	$i(s)$	$j(s)$	$k(s)$
1						0·0	0	0	0
2				r2		−11·6	1	0	0
3			r2			−10·1	1	0	0
4		r2				−10·1	1	0	0
5			r2	r2		−23·7	2	0	0
6		r2		r2		−21·7	2	0	0
7		r2	r2			−22·2	2	0	0
8		r2	r2	r2		−33·8	3	0	0
9				c2		−10·8	0	1	0
10			c2			−10·8	0	1	0
11		c2				−12·1	0	1	0
12			c2	c2		−21·6	0	2	0
13		c2		c2		−22·9	0	2	0
14		c2	c2			−22·9	0	2	0
15		c2	c2	c2		−33·7	0	3	0
16			c2	r2		−22·4	1	1	0
17		c2		r2		−23·7	1	1	0
18		c2	c2	r2		−34·5	1	2	0
19		c2	r2			−22·2	1	1	0
20			r2	c2		−20·9	1	1	0
21		c2	r2	c2		−33·0	1	2	0
22		r2	c2			−20·9	1	1	0
23		r2		c2		−20·9	1	1	0
24		r2	c2	c2		−31·7	1	2	0
25		c2	r2—r2			−35·8	2	1	0
26		r2	c2	r2		−32·5	2	1	0
27		r2—r2		c2		−33·0	2	1	0
28					RNAP	−12·5	0	0	1
29		r2			RNAP	−22·6	1	0	1
30		c2			RNAP	−24·6	0	1	1
31	RNAP		r2			−21·6	1	0	1
32	RNAP		r2—r2			−35·2	2	0	1
33	RNAP		r2	c2		−32·4	1	1	1
34	RNAP					−9·9	0	0	1
35	RNAP			r2		−21·5	1	0	1
36	RNAP			c2		−20·7	0	1	1
37	RNAP		c2			−20·7	0	1	1
38	RNAP		c2	r2		−32·3	1	1	1
39	RNAP		c2	c2		−31·5	0	2	1
40	RNAP				RNAP	−22·4	0	0	2

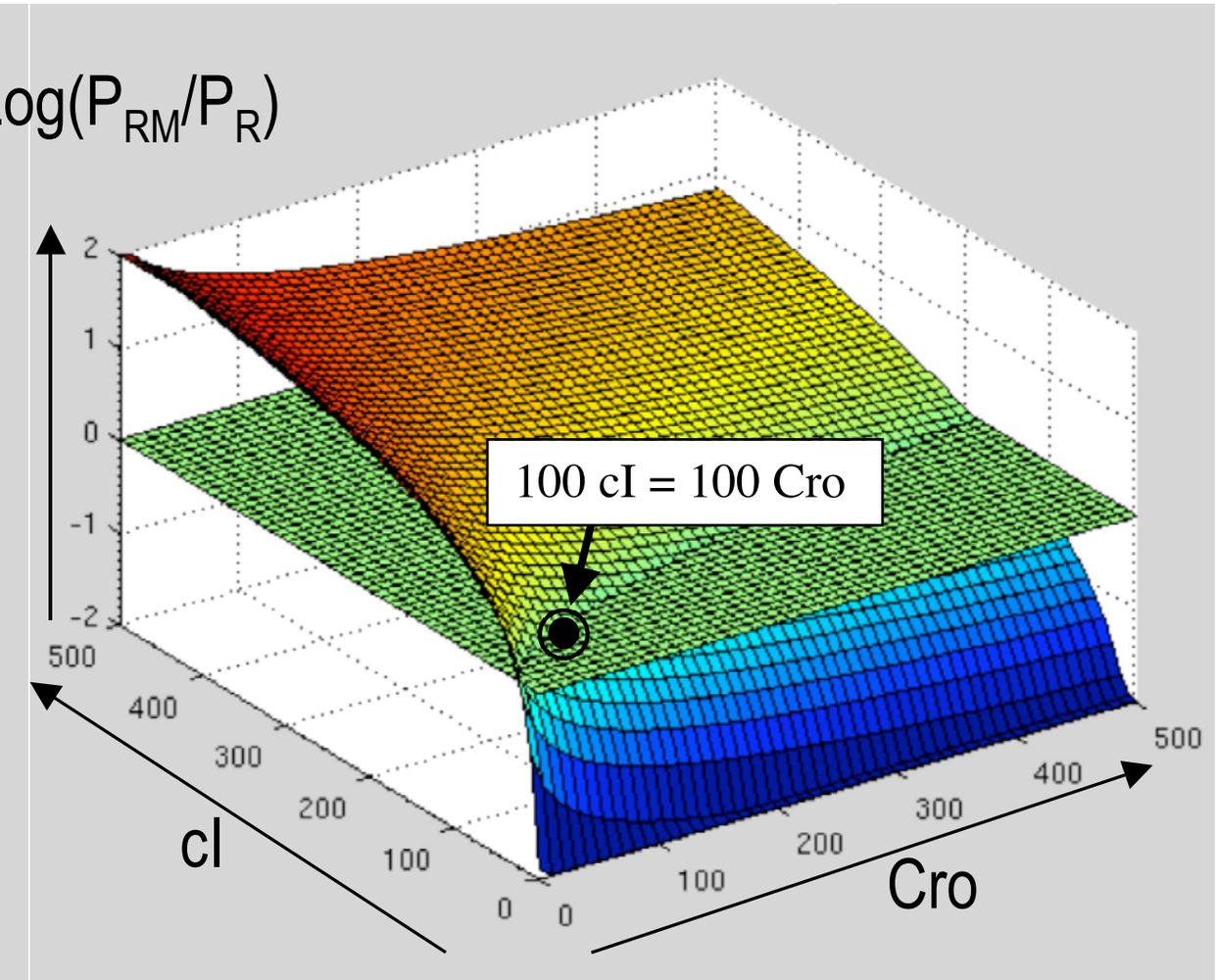

O_R3
O_R2
O_R1
RNA pol
O_R3
O_R2
O_R1
Cro
cI
O_R3
O_R2
O_R1
RNA pol
O_R3
O_R2
O_R1

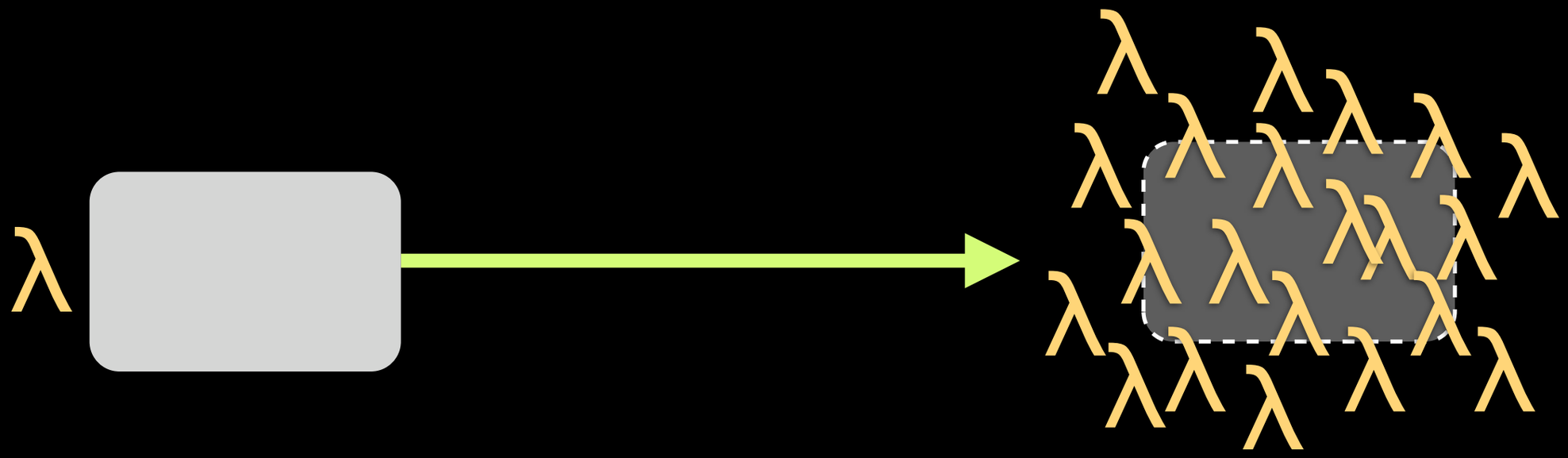
etc.

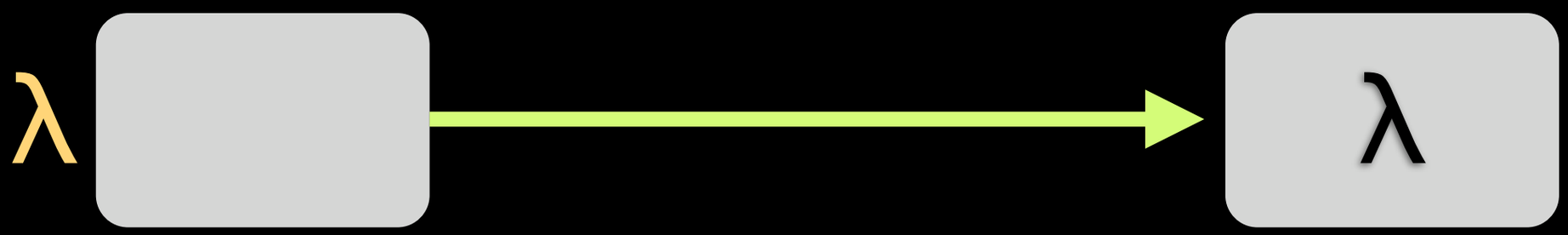
Small bacterium (0.8um^3)



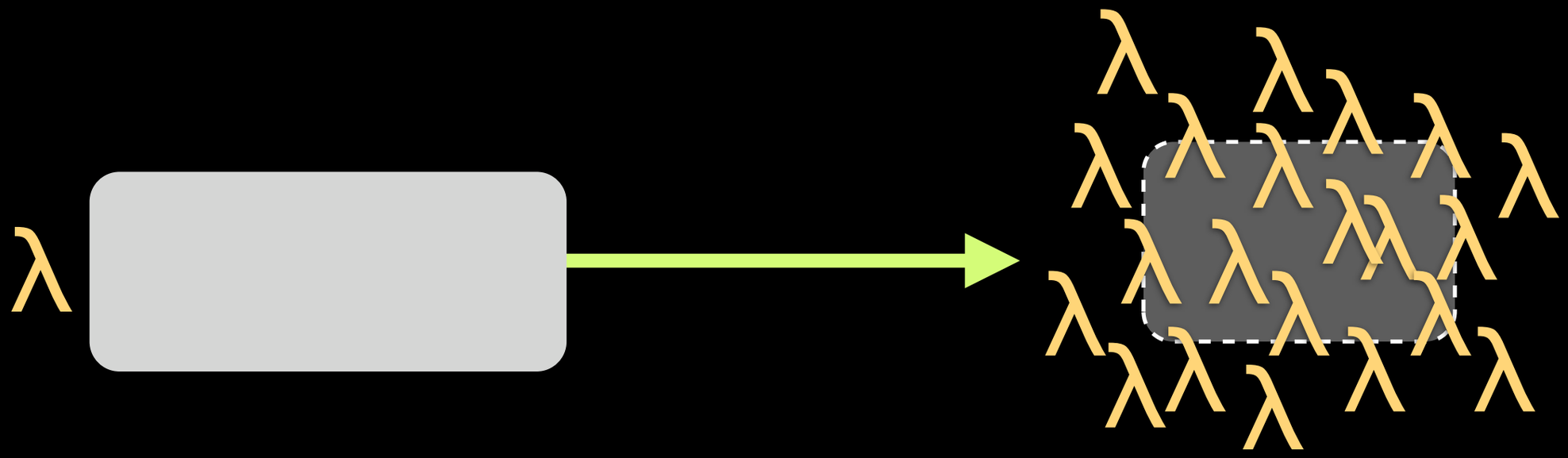
Large bacterium (3 um^3)



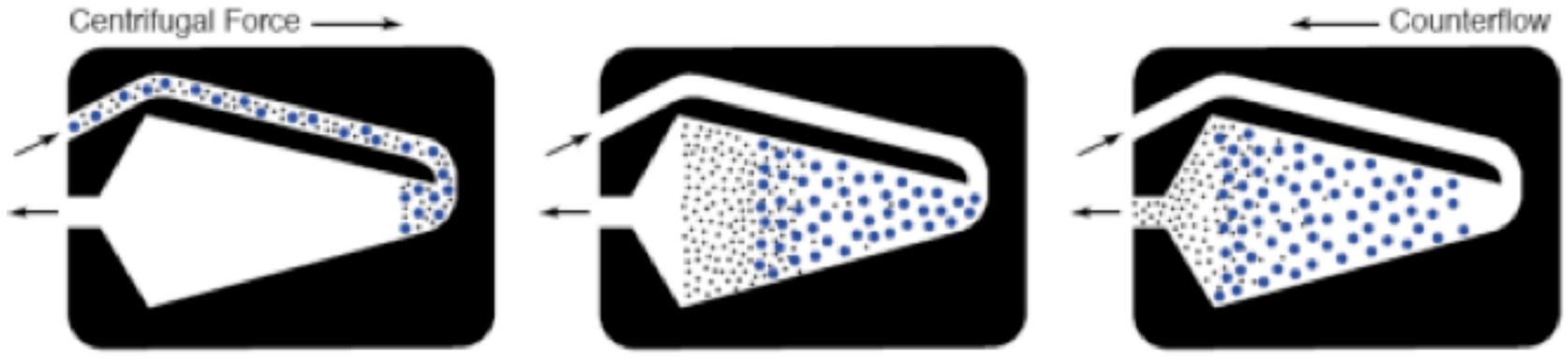




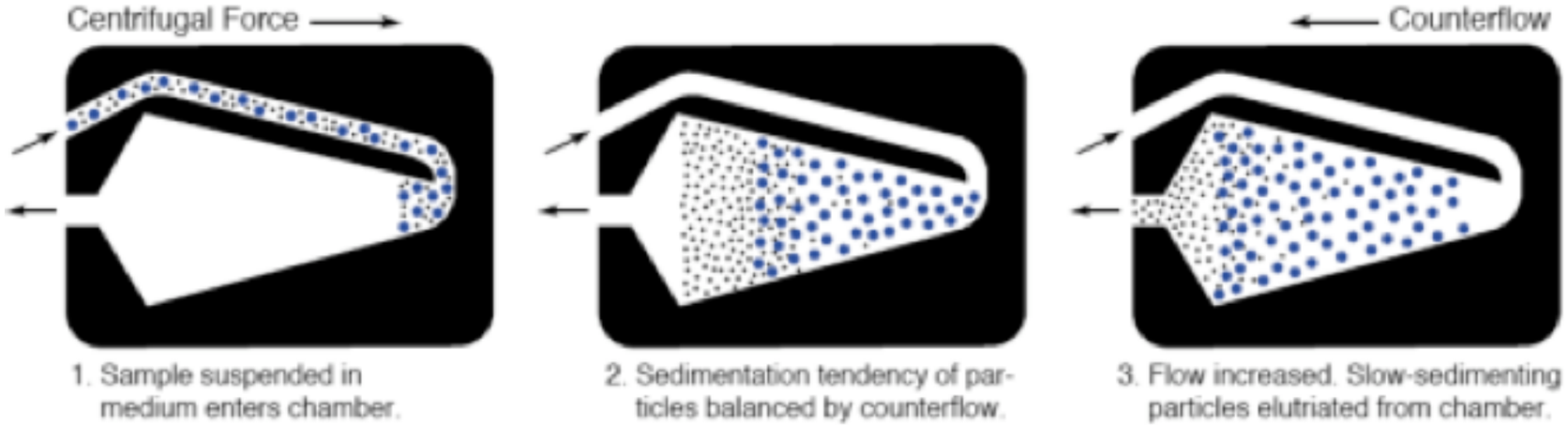
François St-Pierre

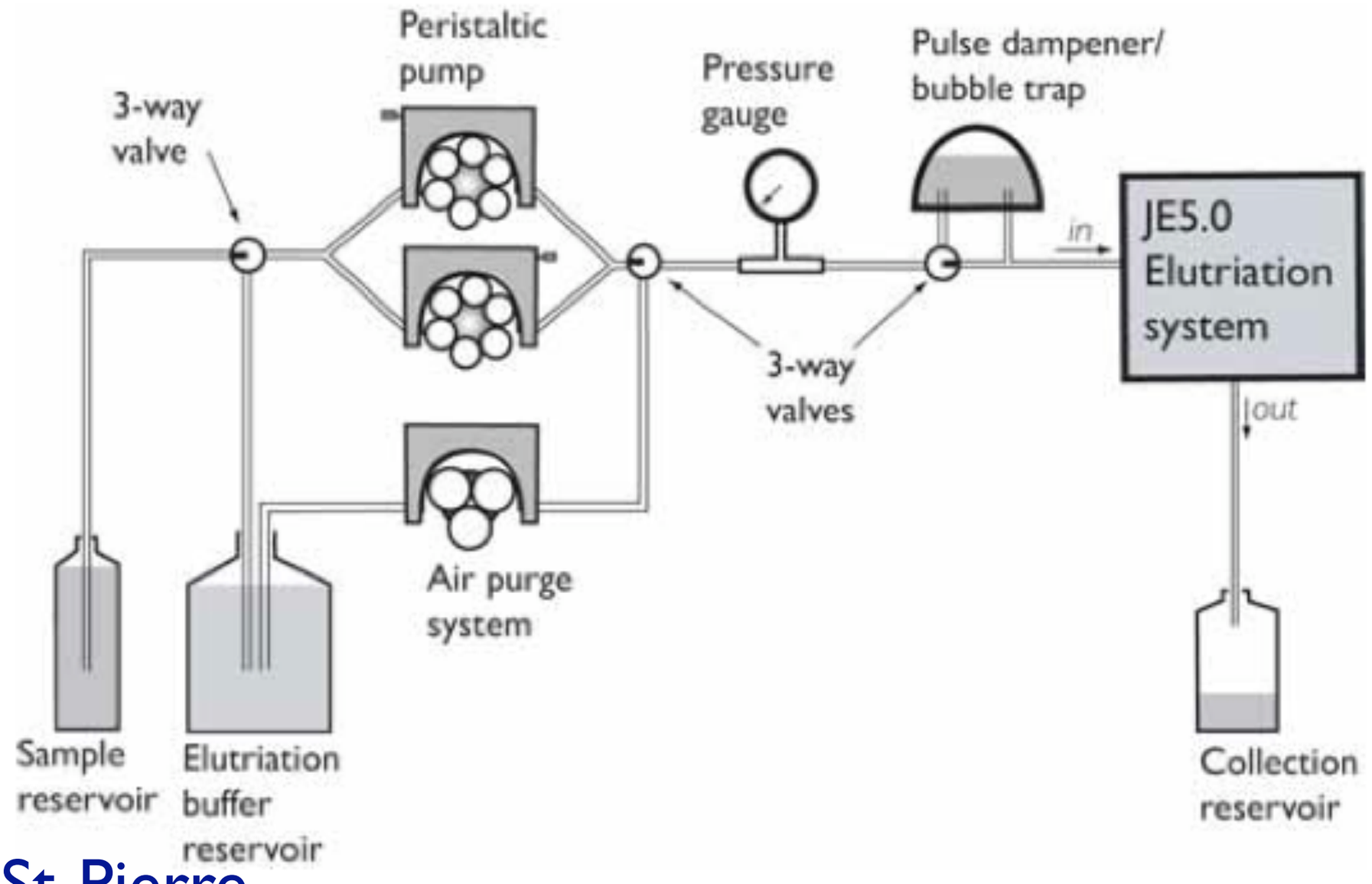


François St-Pierre



François St-Pierre





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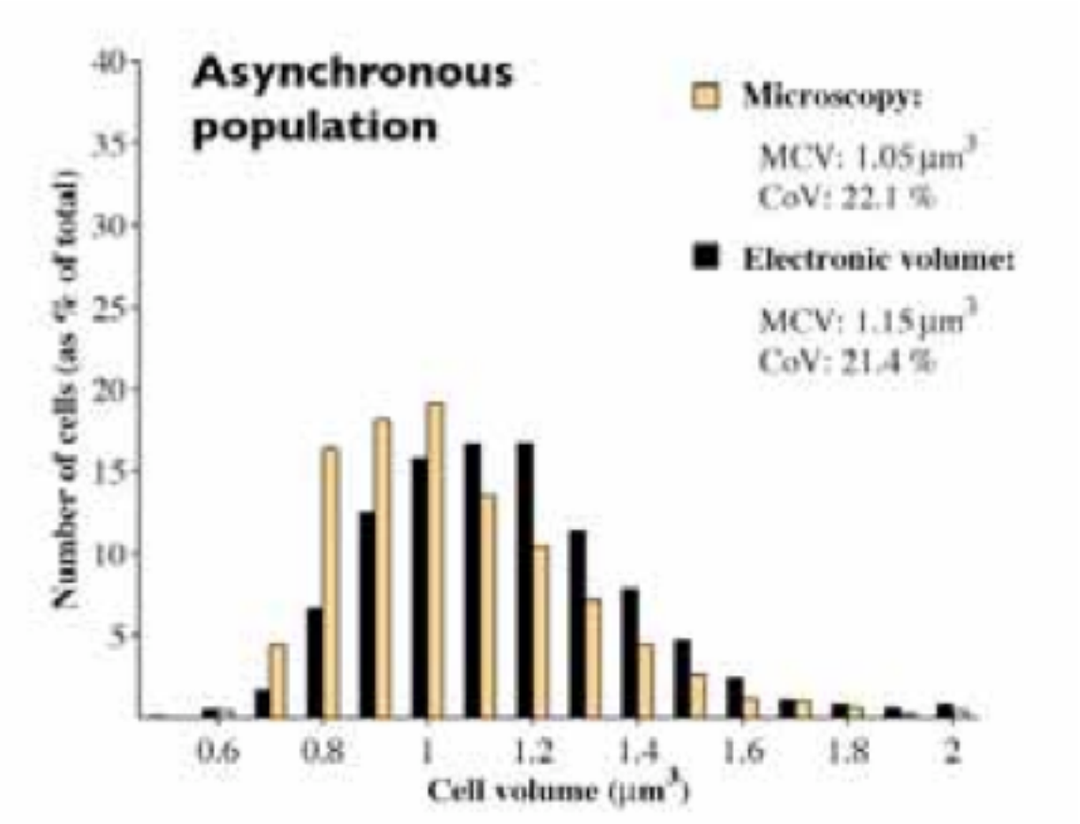

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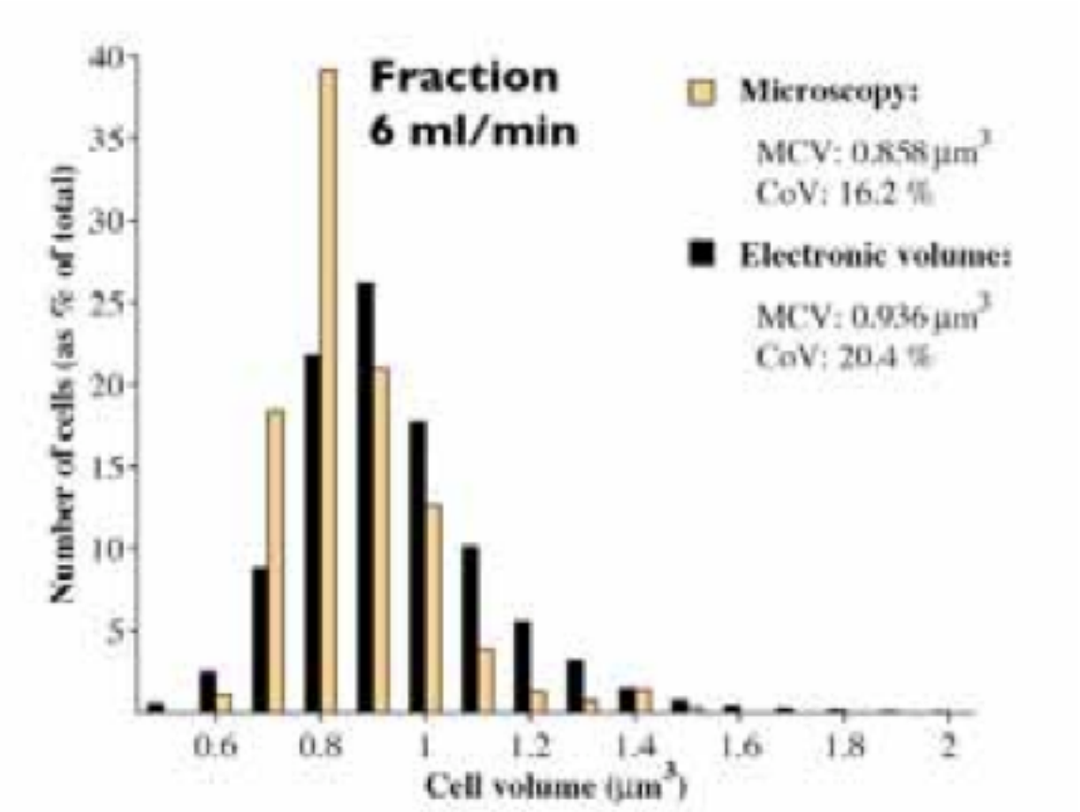
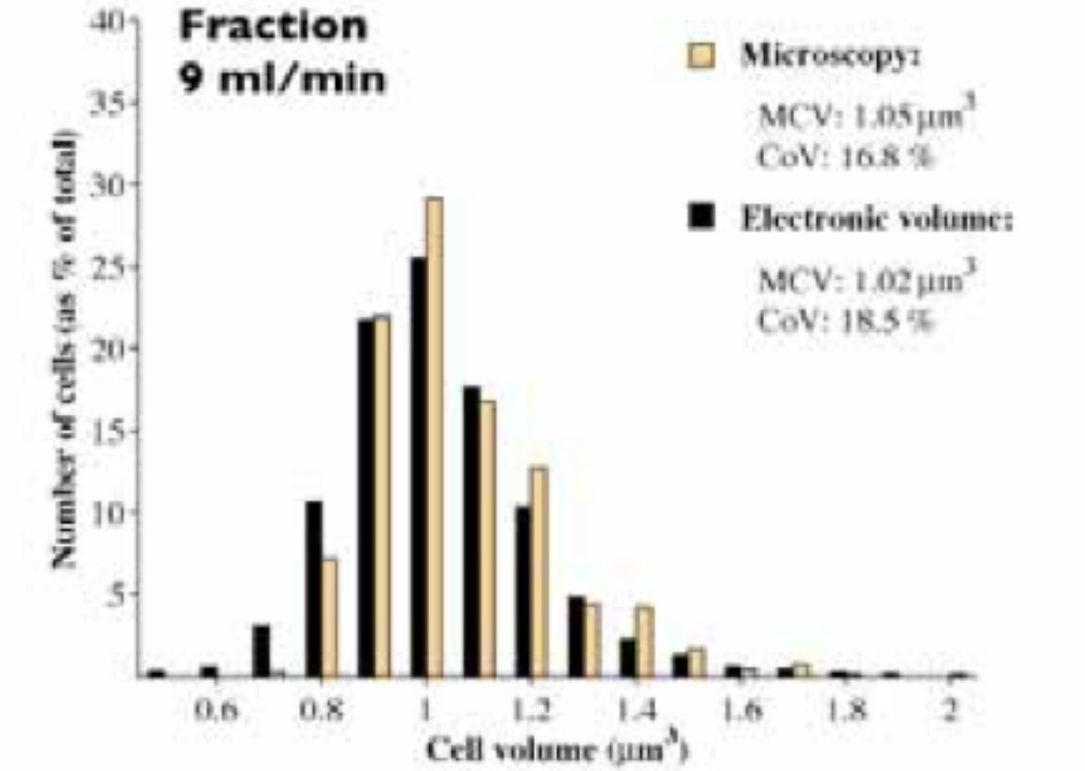
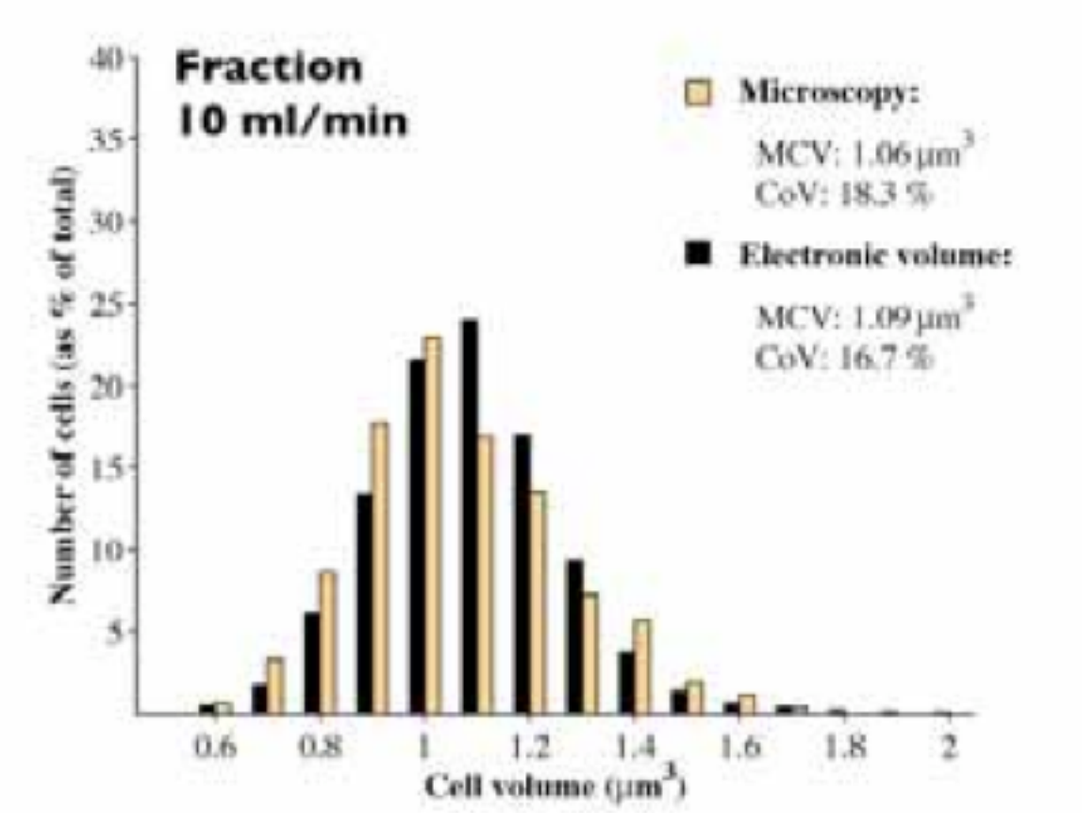


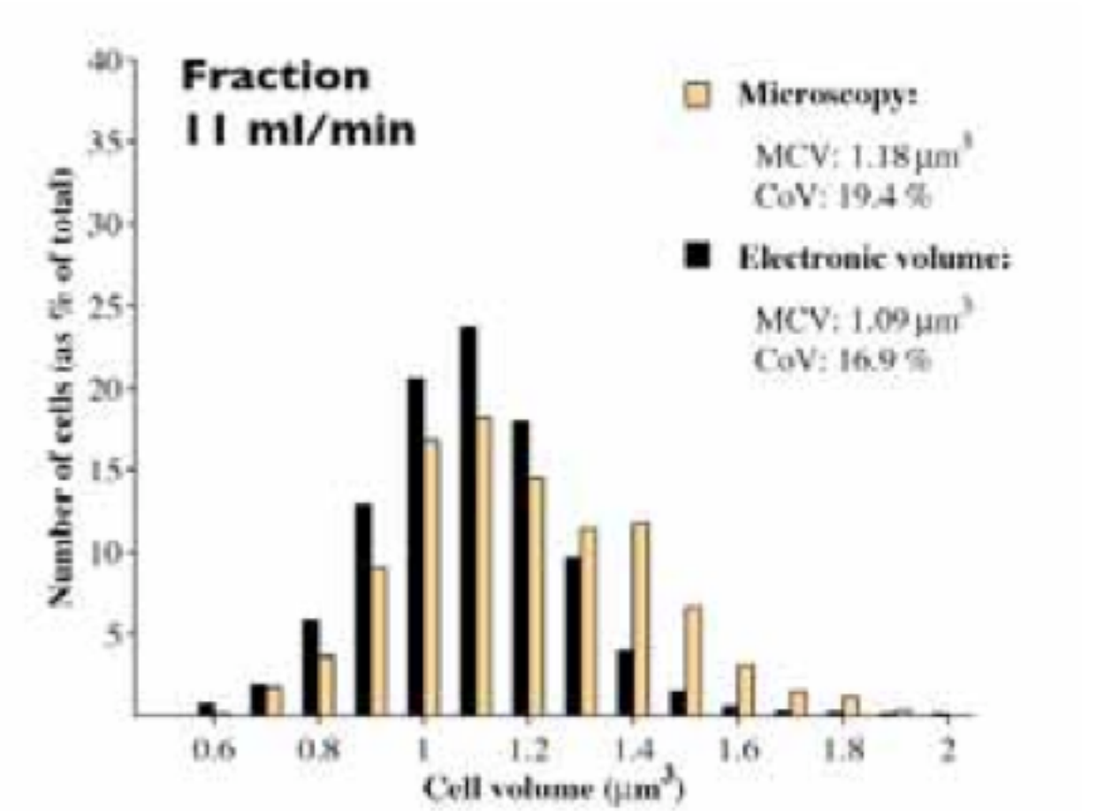
François St-Pierre



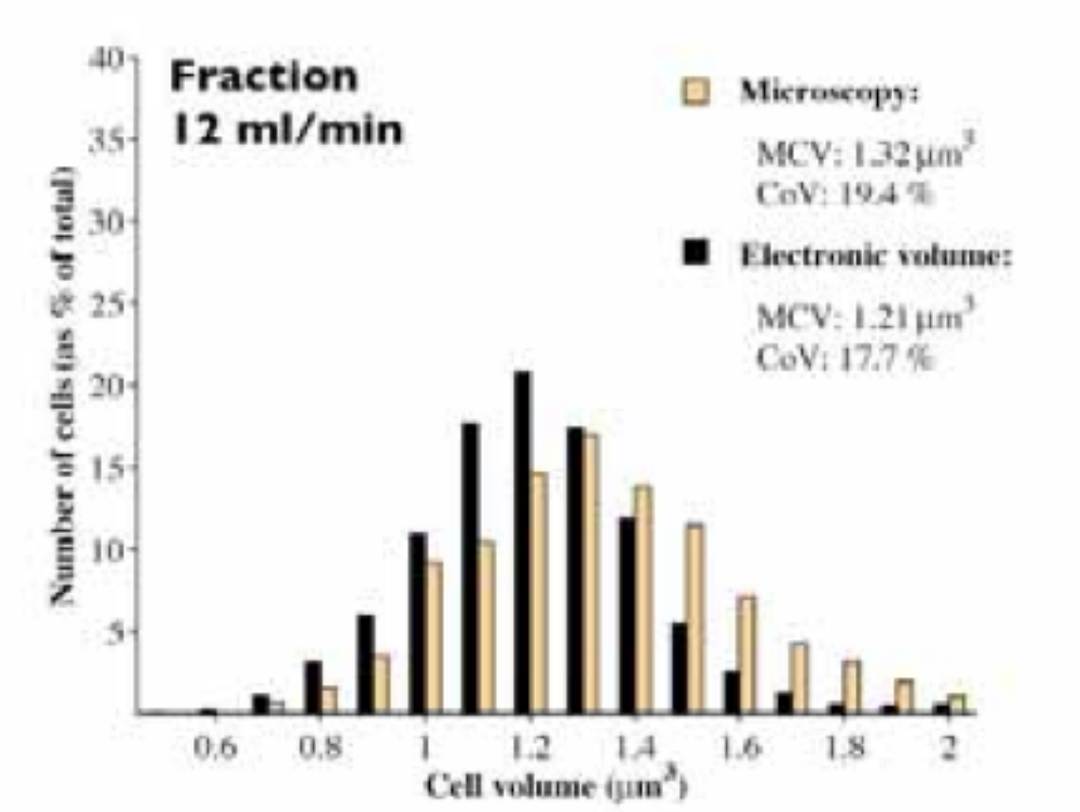
François St-Pierre



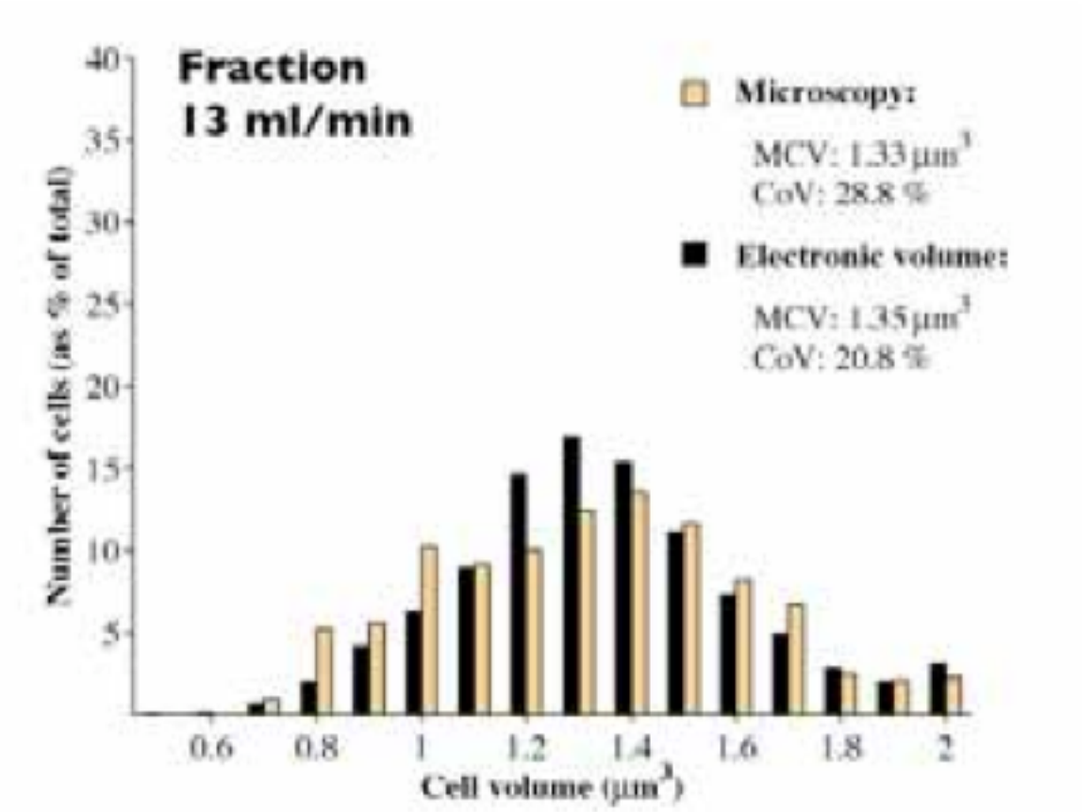
François St-Pierre



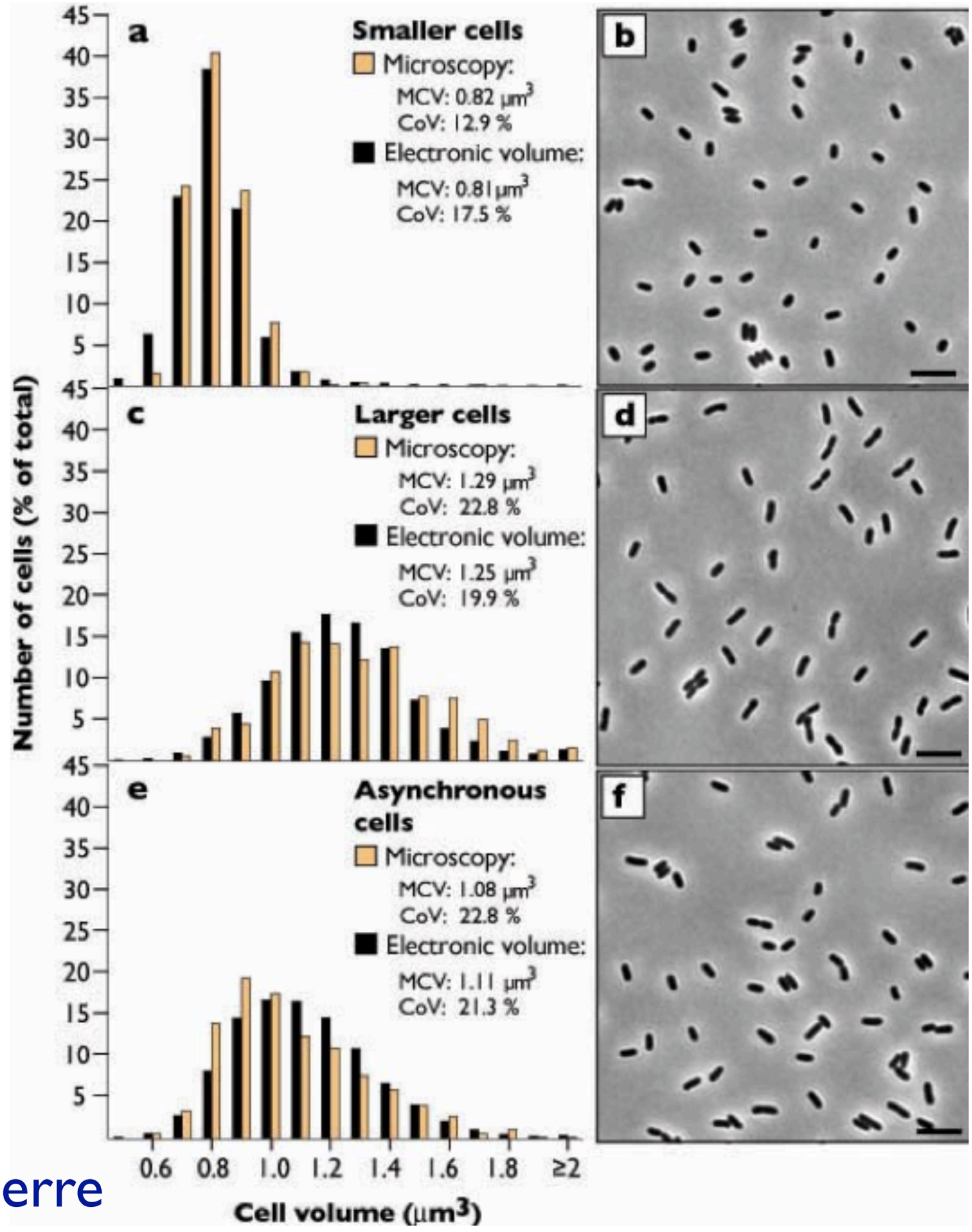
François St-Pierre



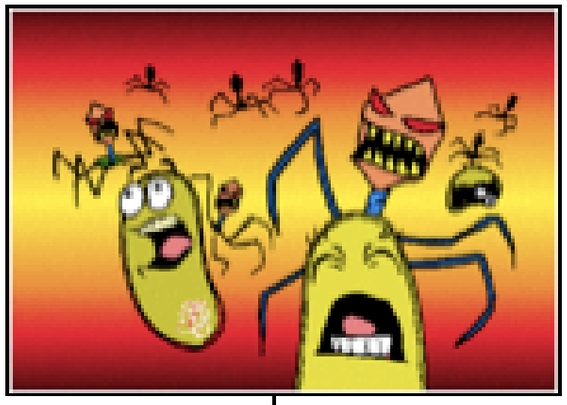
François St-Pierre



François St-Pierre



François St-Pierre

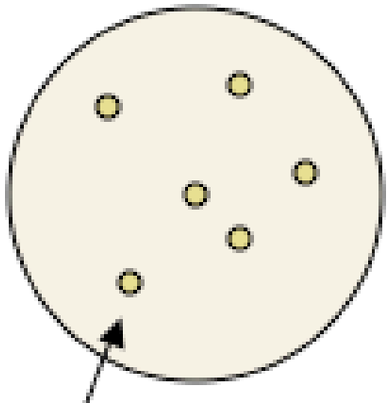


1 Infect with **λ cI857::KanR1** at API=0.005

2 Incubate in TB at 30C for 30min

3 Remove free phages & plate

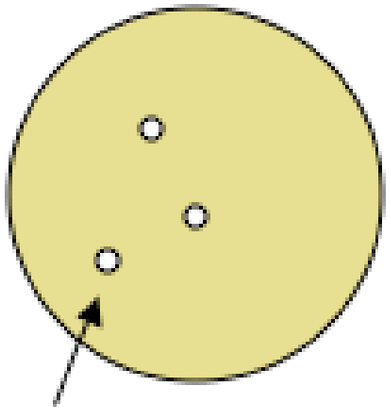
Lysogens
TB-Kan, 30C



Colony

+

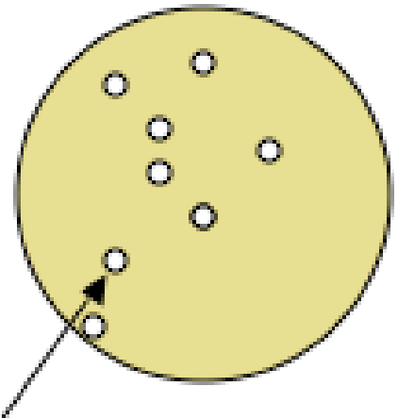
Lytic centers
TB plate, 30C



Plaque

?
=

Infectious centers
TB plate, 42C



Plaque

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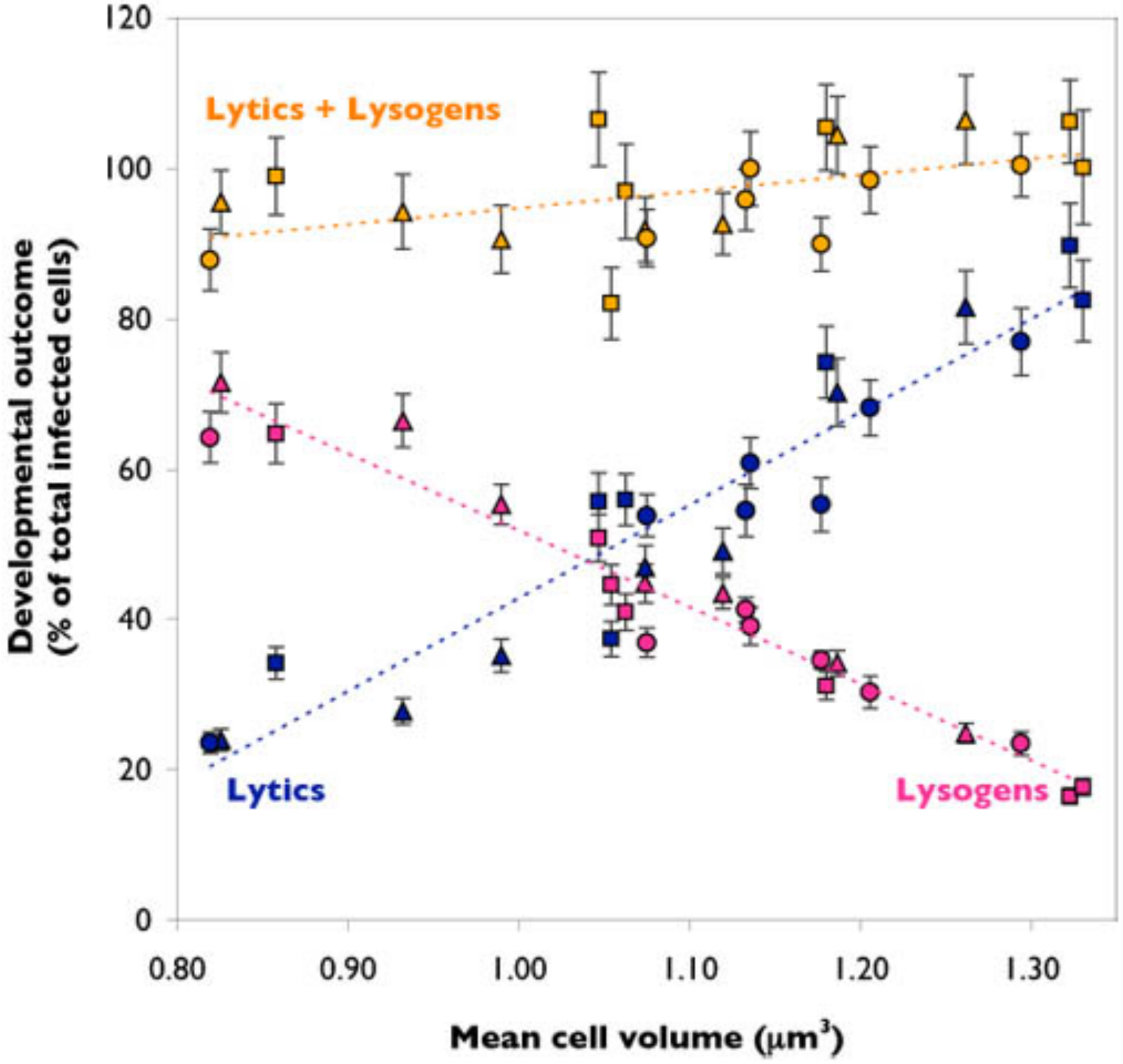
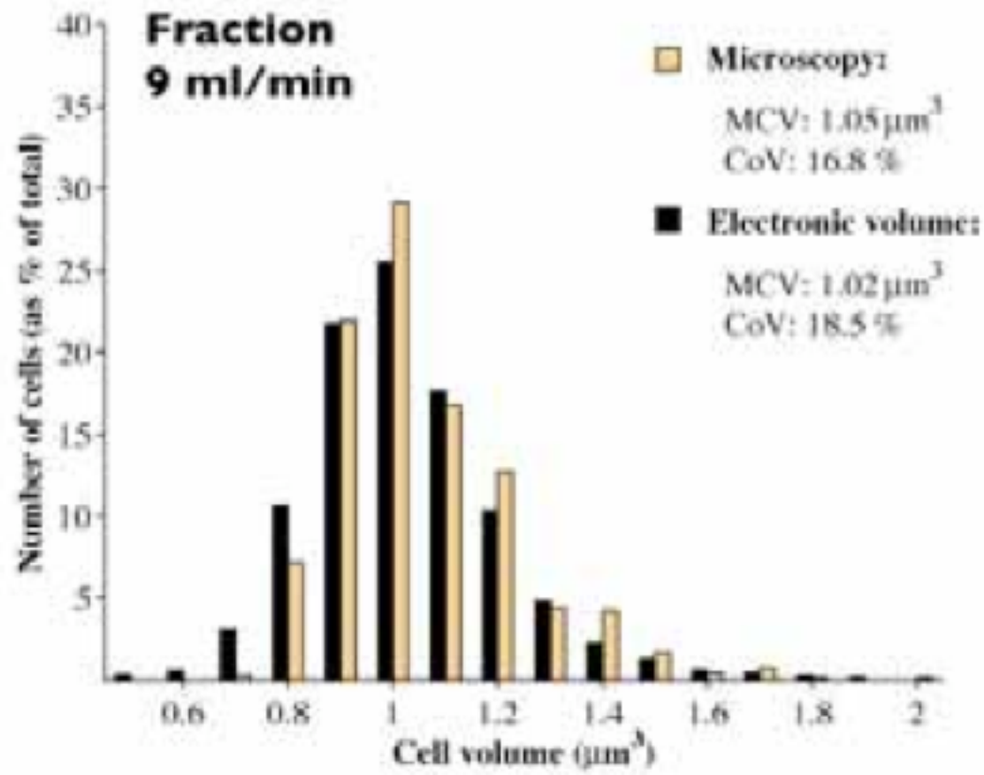


François St-Pierre



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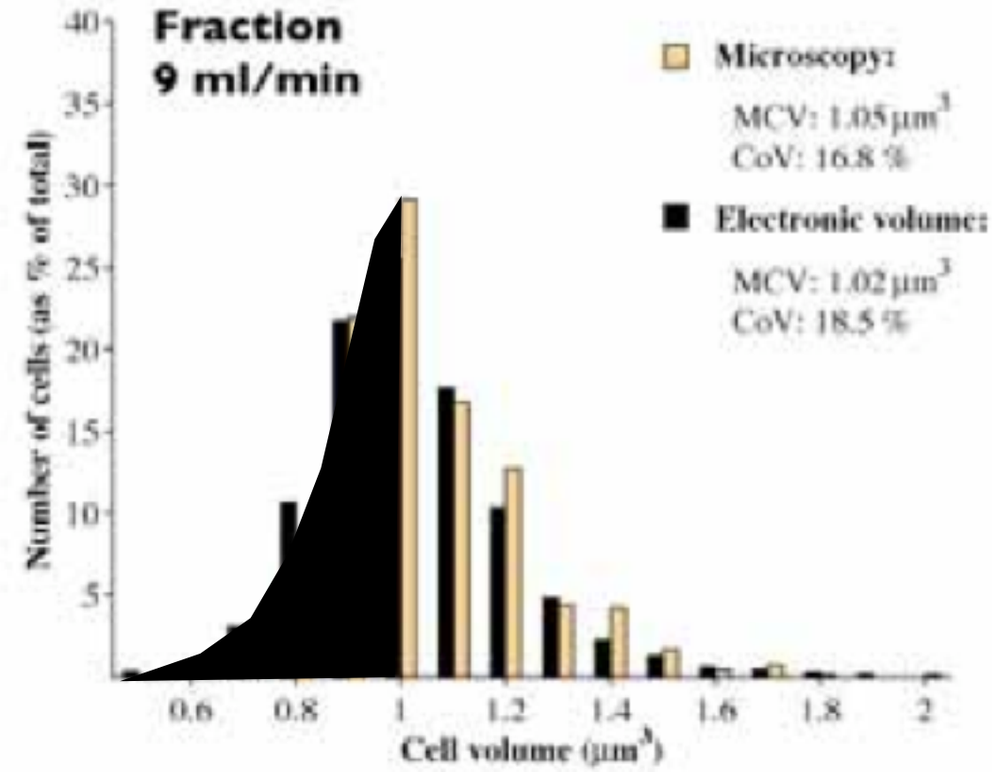
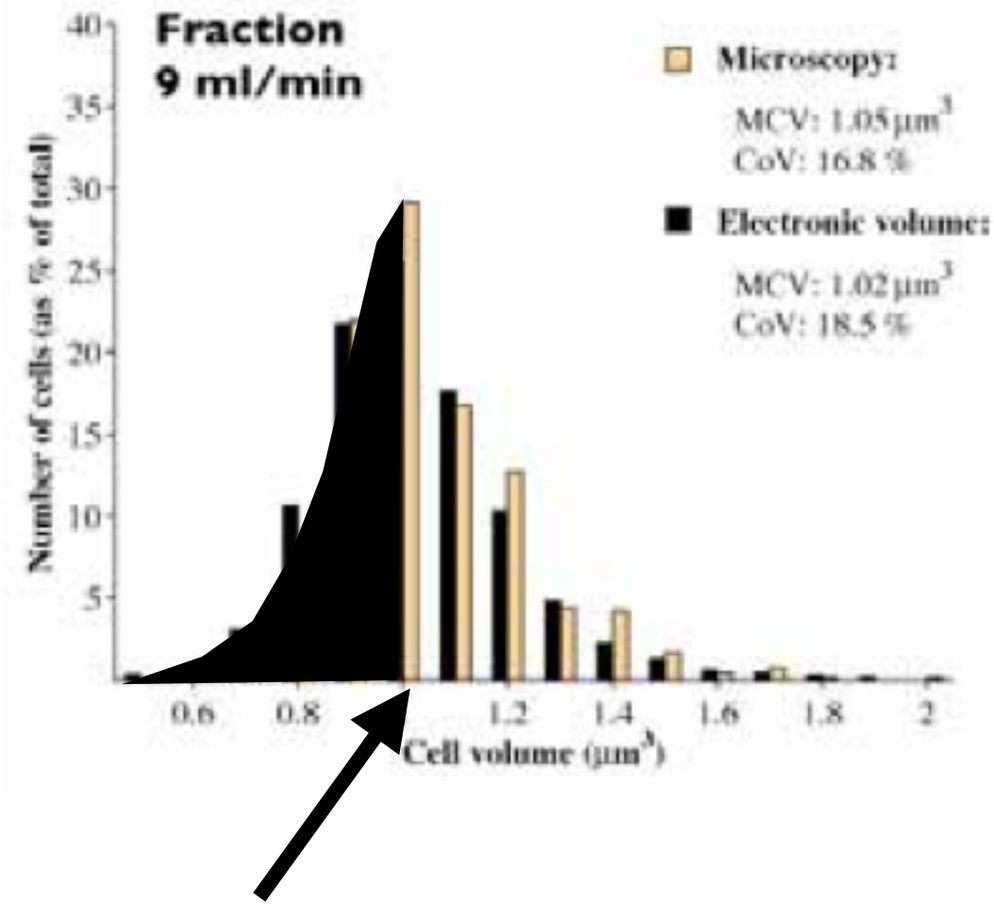
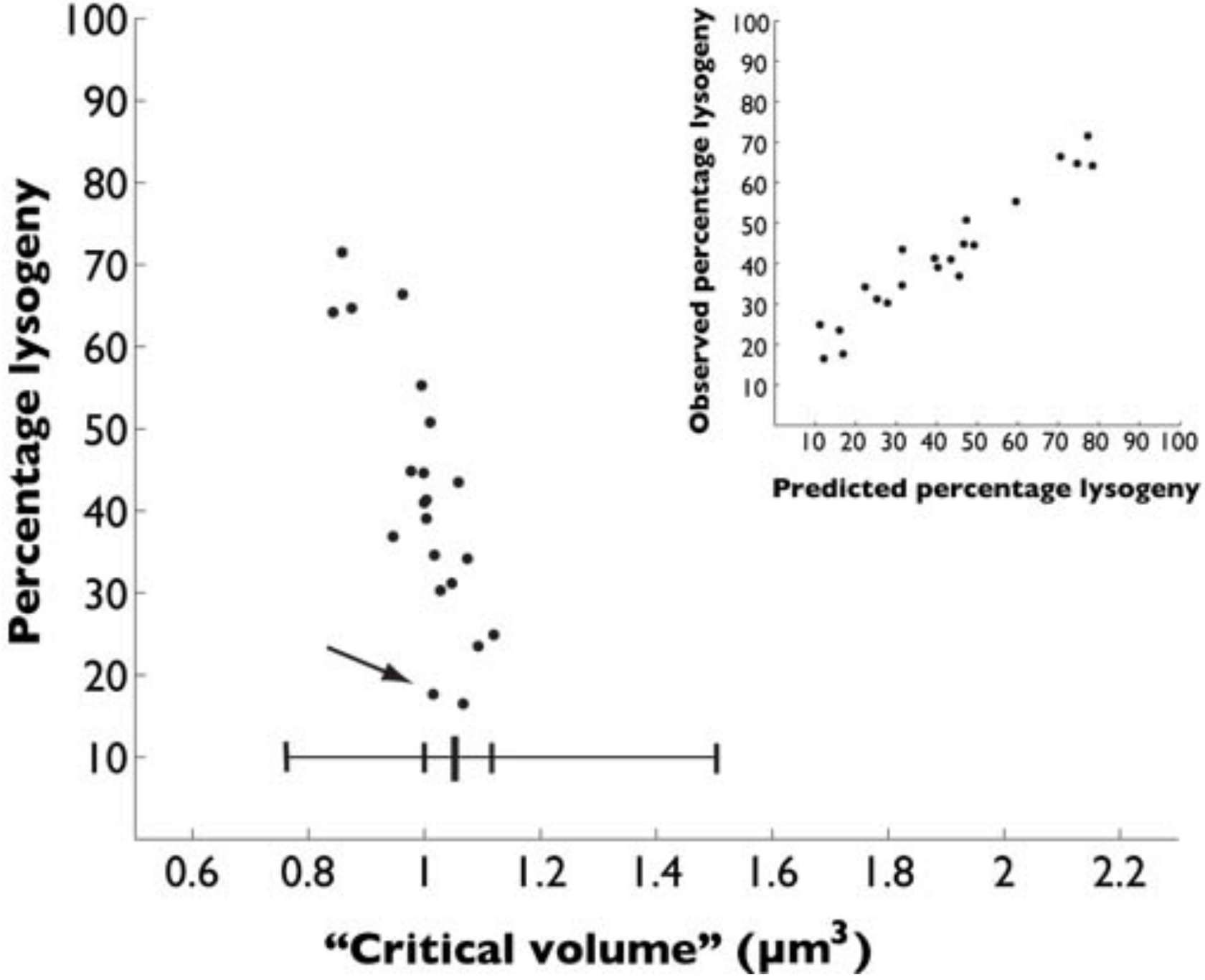

Fraction
9 ml/min
Microscopy:
MCV: 1.05 µm³
CoV: 16.8 %
Electronic volume:
MCV: 1.02 µm³
CoV: 18.5 %
Number of cells (as % of total)
Cell volume (µm³)
40
35
30
25
20
15
10
5
0.6
0.8
1
1.2
1.4
1.6
1.8
2



"Critical" volume for this fraction
(compute for all fractions)



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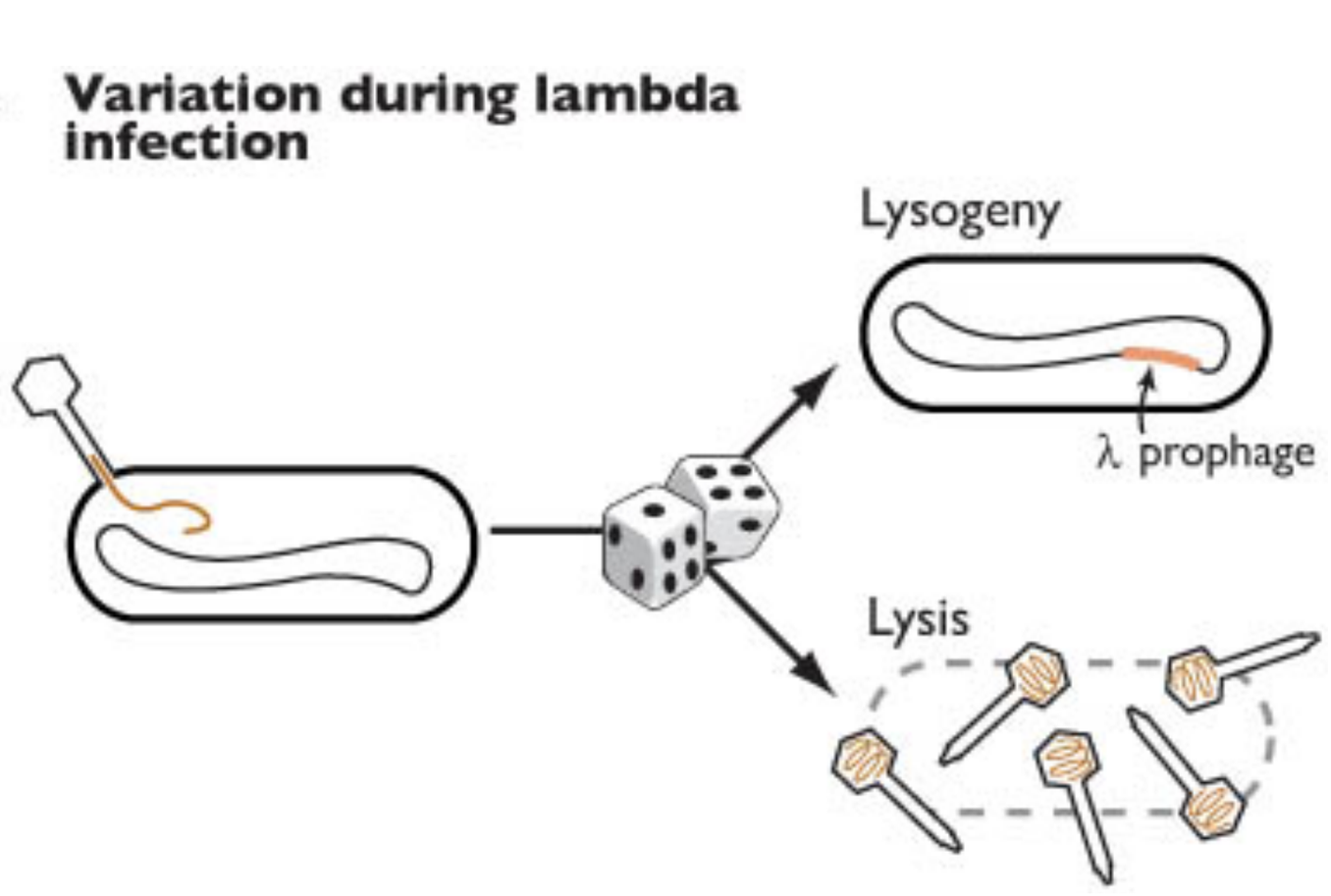

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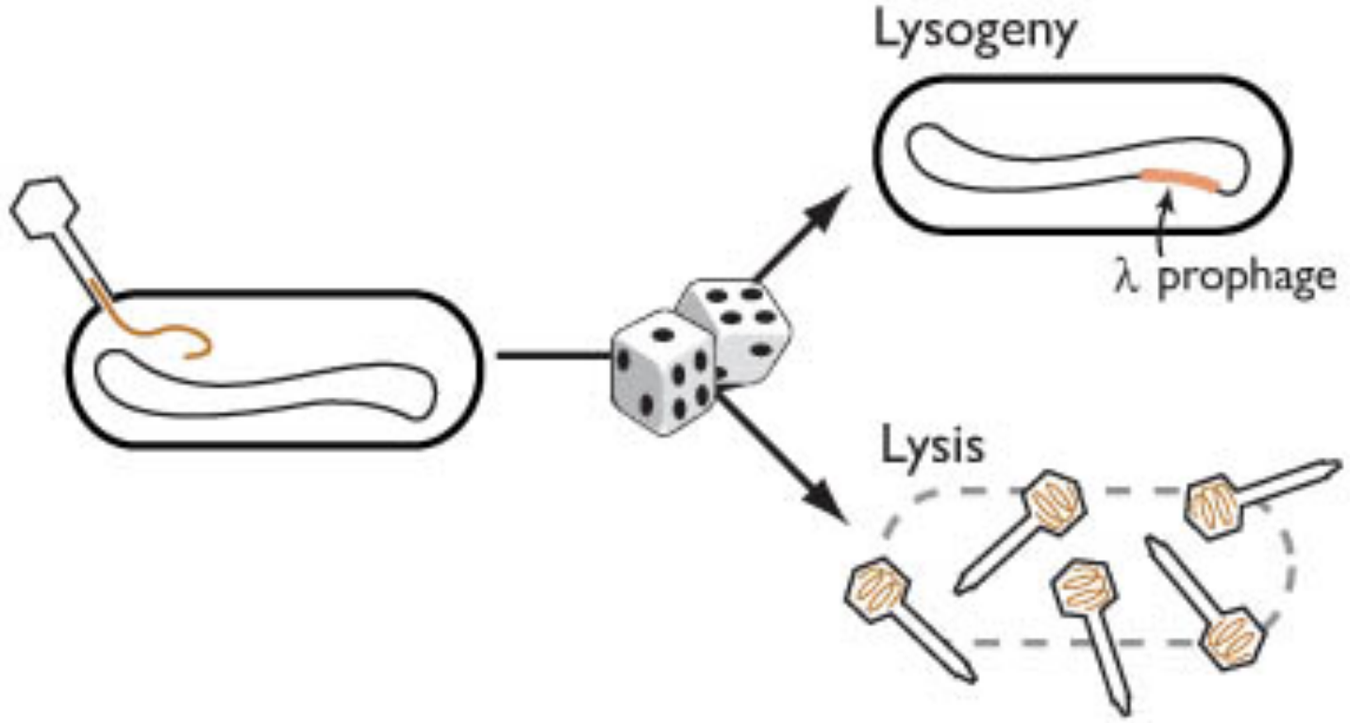
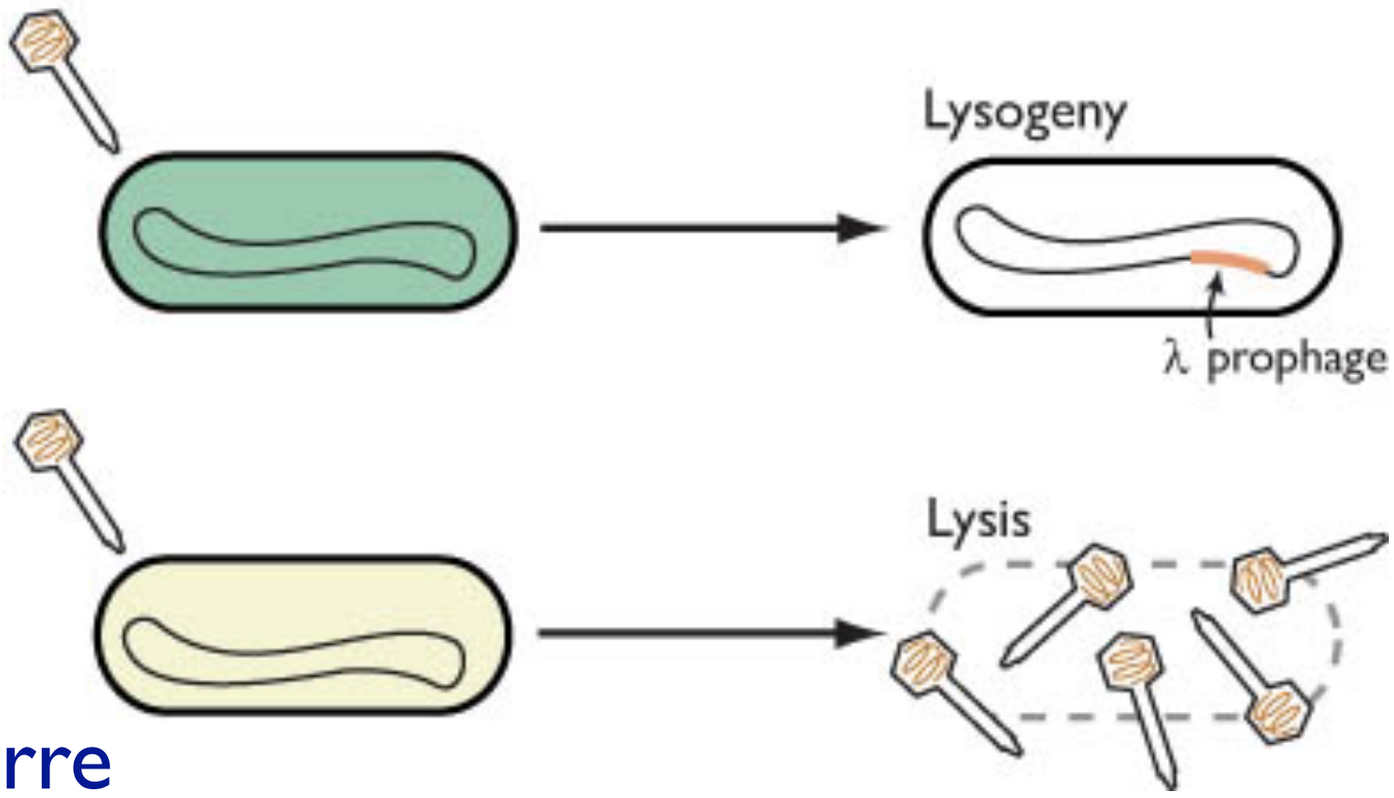
a Variation during lambda infection



b Variation prior to lambda infection



François St-Pierre

Show single cell movies!

François St-Pierre