

# François & Hakim

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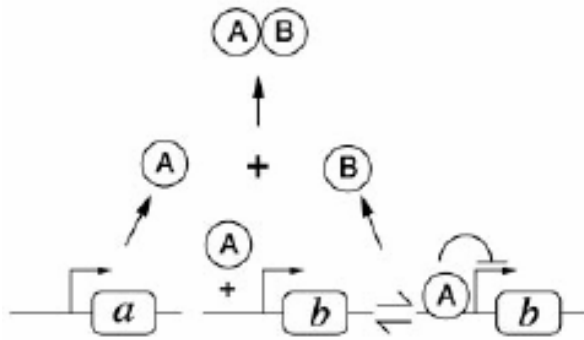
2005-02

[www.luca.demon.co.uk](http://www.luca.demon.co.uk)

# François & Hakim Fig3A

PNAS (101)2, 580-585, 2004

Design of genetic networks with specified functions by evolution in silico



Reactions	Constants	Stability
$a \rightarrow a+A$	0.20	0.9-1.4
$A \rightarrow \text{Nothing}$	0.0085	0.0-1.5
$b \rightarrow b+B$	0.37	0.7-1.3
$B \rightarrow \text{Nothing}$	0.034	0.0-8.9
$A+B \rightarrow A:B$	0.72	0.1 - > 10
$A:B \rightarrow \text{Nothing}$	0.53	Irrelevant
$b+A \rightarrow b:A$	0.19	0.7-7.6
$b:A \rightarrow b+A$	0.42	0.2-1.5
$b:A \rightarrow b:A+B$	0.027	0.0-2.3

Fig 3A

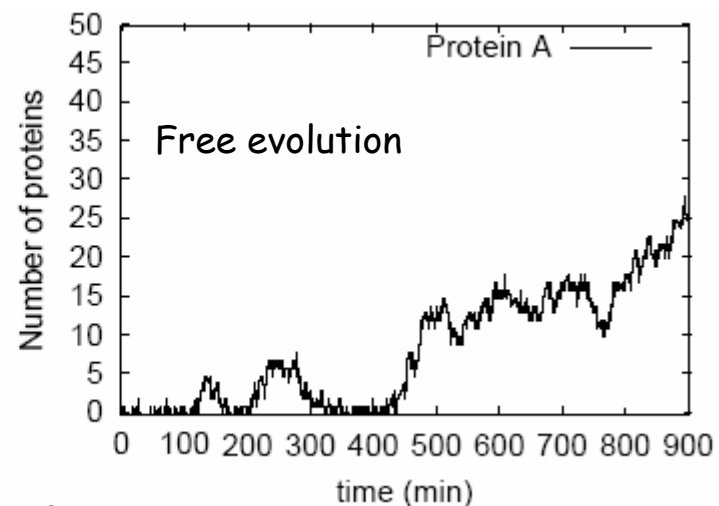
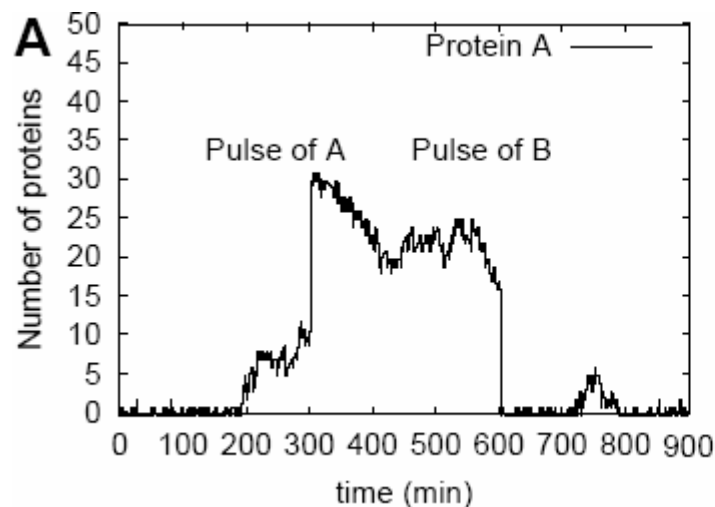
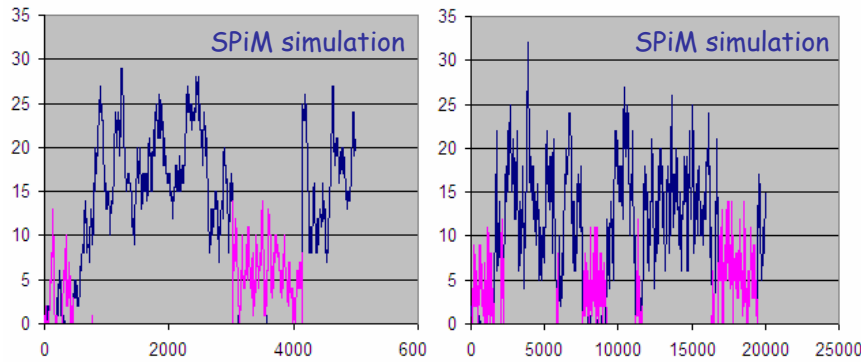


Fig 14A

# François & Hakim Fig3A, SPiM simulation

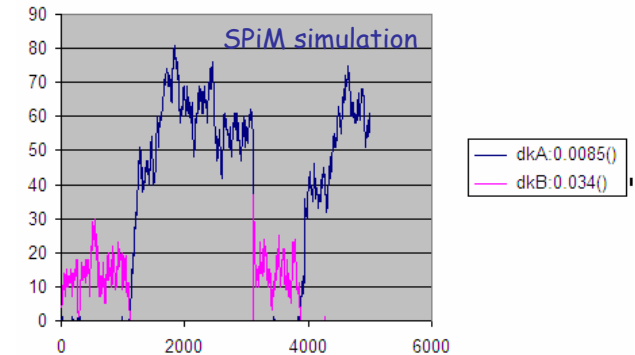
Parameters as in paper



Spontaneous switch at ~500  
(as discussed in Supporting Text)  
30xB injected at ~3000  
30xA injected at ~4000

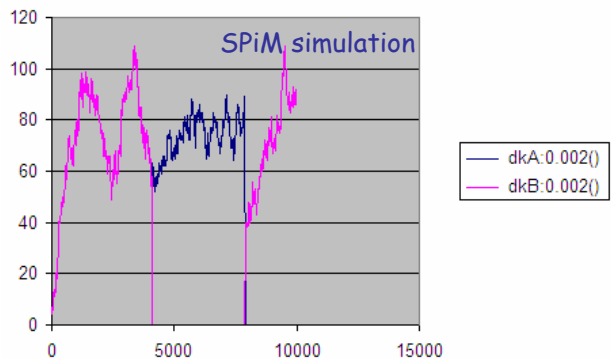
Free evolution

3 copies of each gene.

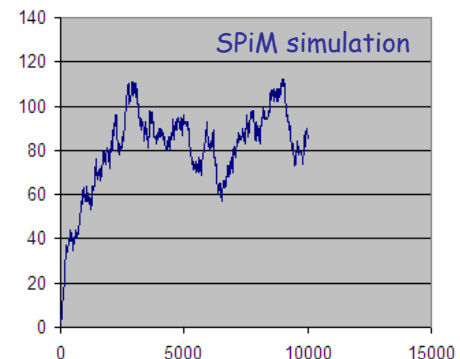


Spontaneous switch at ~1100  
100xB injected at ~3000  
30xA injected at ~4000

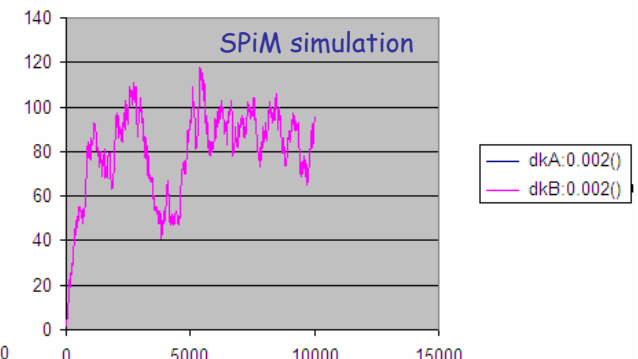
Modified for stability:  $dkA = 0.02$ ,  $dkB = 0.02$



120xA injected at ~4000  
120xB injected at ~8000



Free evolution



# François & Hakim Fig3Ast8

Circuit of Fig 3A with parameters from SupportingText Fig 8, plotted in Fig 13A

Reactions	Constants
$a \rightarrow a+A$	0.52
$A \rightarrow \text{Nothing}$	0.00019
$b \rightarrow b+B$	0.79
$B \rightarrow \text{Nothing}$	0.0030
$A+B \rightarrow A:B$	0.053
$A:B \rightarrow \text{Nothing}$	0.15
$b+A \rightarrow b:A$	0.22
$b:A \rightarrow b+A$	0.31
$b:A \rightarrow b:A+B$	0.43

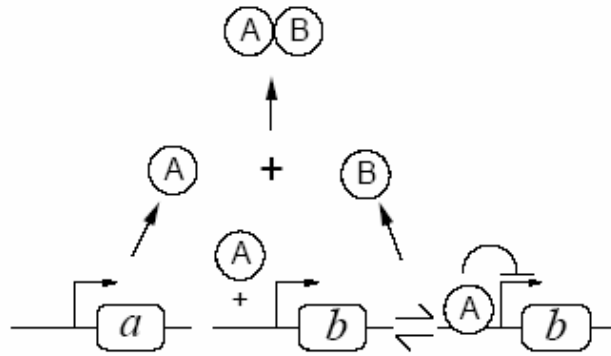


Fig 8

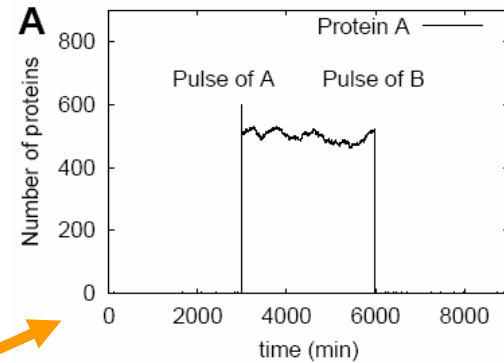
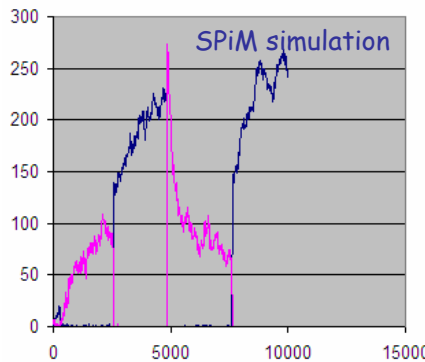
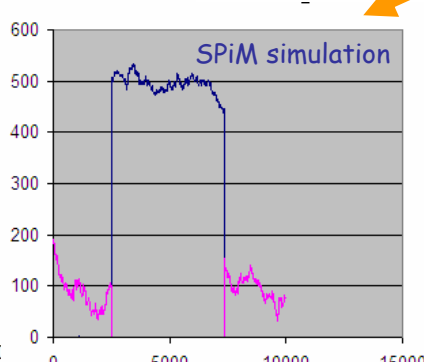


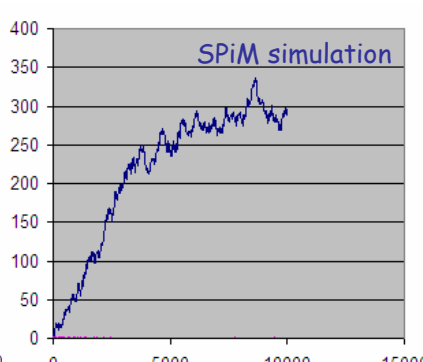
Fig 13A



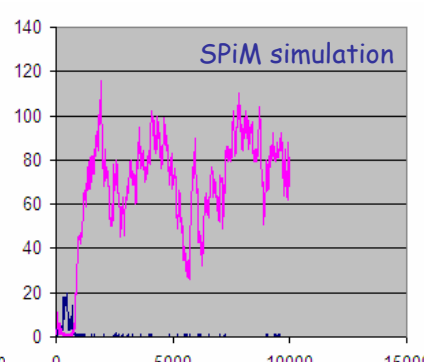
200xA injected at ~2500  
500xB injected at ~5000  
200xA injected at ~7500



200xB injected at 0  
600xA injected at ~2500  
600xB injected at ~7500



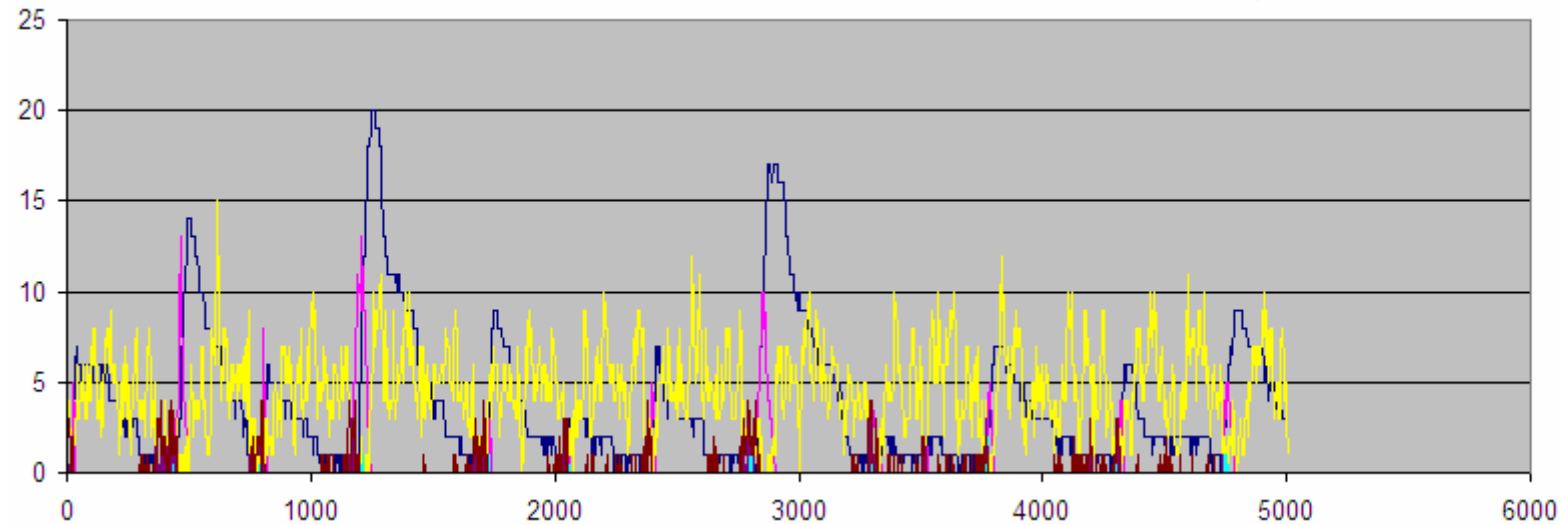
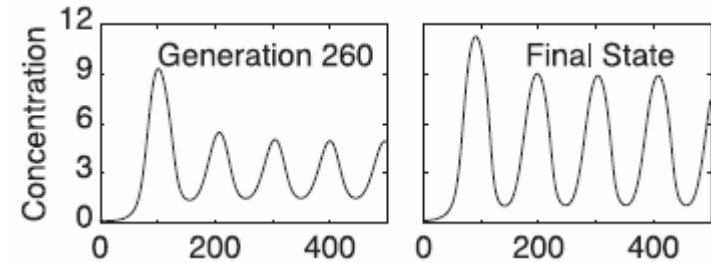
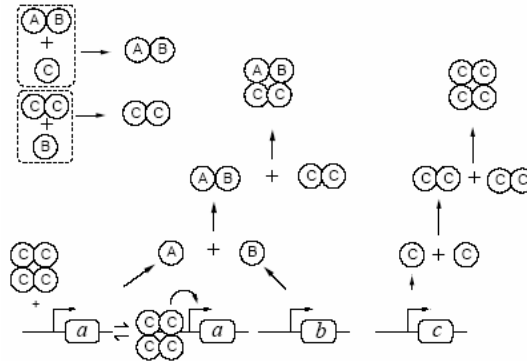
Free evolution



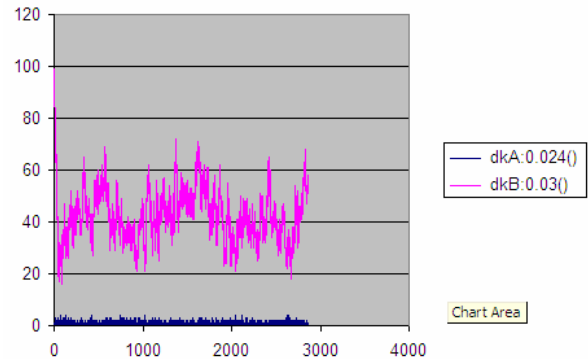
— dkA:0.00019()  
— dkB:0.003()

# François & Hakim Fig4&15

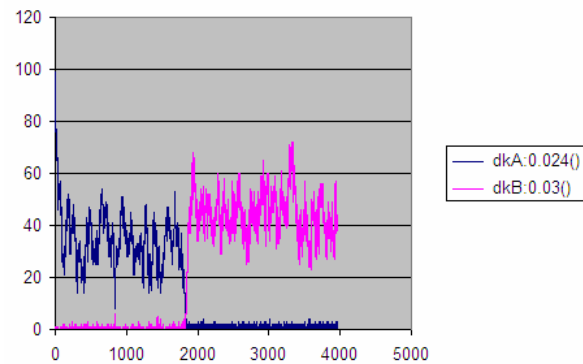
Reactions	Constants
$a \rightarrow a+A$	0
$A \rightarrow \text{Nothing}$	0.00019
$b \rightarrow b+B$	0.43
$B \rightarrow \text{Nothing}$	0.077
$c \rightarrow c+C$	0.57
$C \rightarrow \text{Nothing}$	0.023
$A+B \rightarrow A:B$	0.066
$A:B \rightarrow \text{Nothing}$	0.057
$C+C \rightarrow C:C$	0.14
$C:C \rightarrow \text{Nothing}$	0.0014
$C:C + B \rightarrow C:C$	0.21
$C:C + C:C \rightarrow C:C:C:C$	0.37
$C:C:C:C \rightarrow \text{Nothing}$	0.24
$C+A:B \rightarrow A:B$	1.5
$a + C:C:C:C \rightarrow a:C:C:C$	0.5
$a:C:C:C \rightarrow a + C:C:C$	0.33
$a:C:C:C \rightarrow a:C:C:C+A$	0.56
$A:B+C:C \rightarrow A:B:C:C$	0.74



# Francois & Hakim 3B



Parameters as in paper.  
Initially:  $1 \times A$ ,  $100 \times B$ ,  
3 copies of each gene.



Parameters as in paper.  
Initially:  $100 \times A$ ,  $1 \times B$ ,  
3 copies of each gene.

Not really bistable.

# François & Hakim 3A in Stochastic- $\pi$

```
(* Francois and Hakim circuit 3A *)  
  
val pntAunb = 0.42  
val geneACst = 0.20  
val geneBCst = 0.37  
val geneBInh = 0.027  
val bA = 0.19  
val AB = 0.72  
val dKA = 0.0085  
val dKB = 0.034  
val dkAB = 0.53  
  
def ptnA[] =  
  (new unb@pntAunb  
   sum delay@dKA + AB! + bA!unb;(unb?= ptnA[]))  
  
def ptnB[] =  
  sum delay@dKB + AB?=cpxAB[]  
  
def cpxAB[] = delay@dkAB  
  
def geneA[] =  
  delay@geneACst; (ptnA[] | geneA[])  
  
def geneBfree[] =  
  sum delay@geneBCst; (ptnB[] | geneBfree[])  
  + bA?unb= geneBbound[unb])  
  
and geneBbound[unb:^[]] =  
  sum delay@geneBInh; (ptnB[] | geneBbound[unb])  
  + unb!; geneBfree[])  
  
run (geneA[] | geneBfree[])
```