Catalytic DNA Systems

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Outline

Catalytic DNA systems – Why are they interesting?
Reaction mechanisms for engineering DNA reaction networks
Some catalytic DNA-based systems
- A catalytic system driven by base paring
- A catalytic system driven by entropy increase
- A catalytic cascade analogous to signaling cascades
- An autocatalytic system

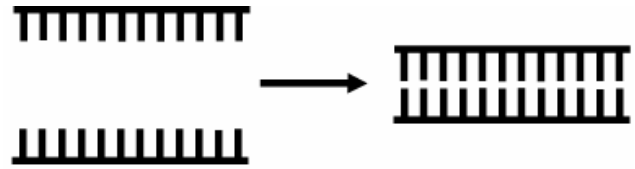
Catalytic DNA systems – Why are they interesting?

Catalytic DNA systems are useful for devising

- DNA-based autonomous motors
  - analogous to biological molecular motors
- DNA-based chemical amplifiers
  - analogous to biological signaling cascades
- DNA-based self-replicating systems
  - analogous to living organisms

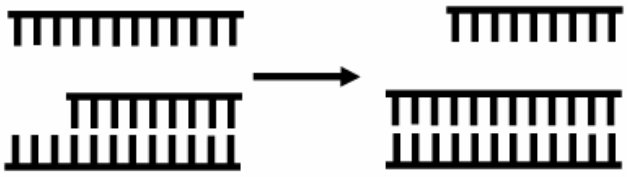
Reaction mechanism for engineering DNA reaction networks

Hybridization



Driven forward by increase in the number of base pairs

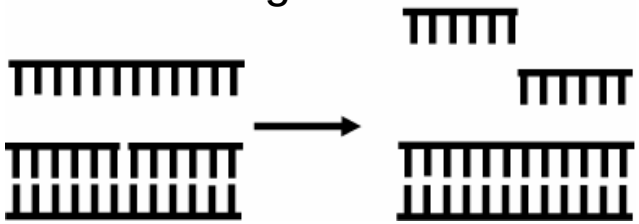
Toehold mediated strand displacement



Toehold or overhang

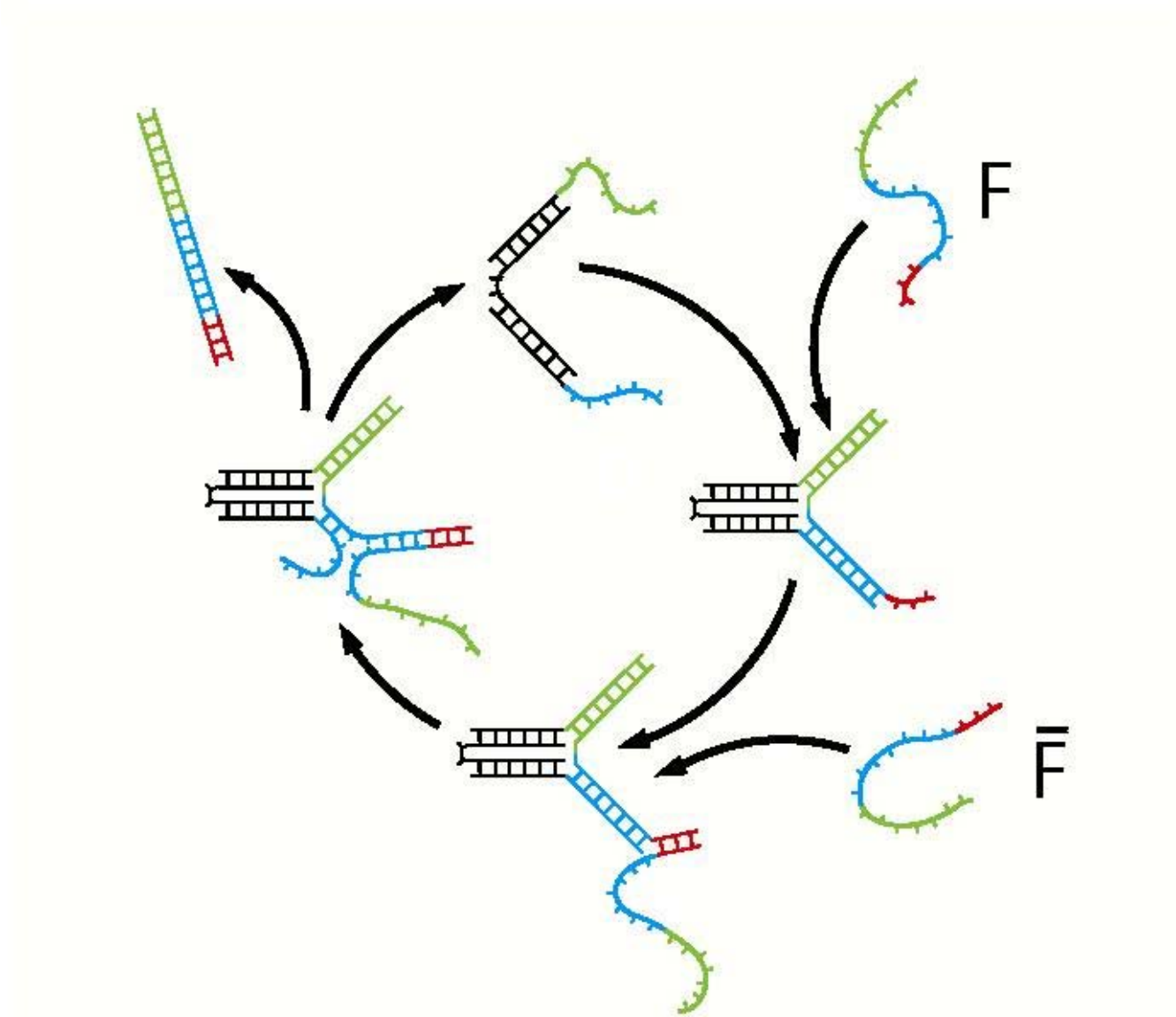
Driven forward by increase in the number of base pairs

Entropy driven strand displacement



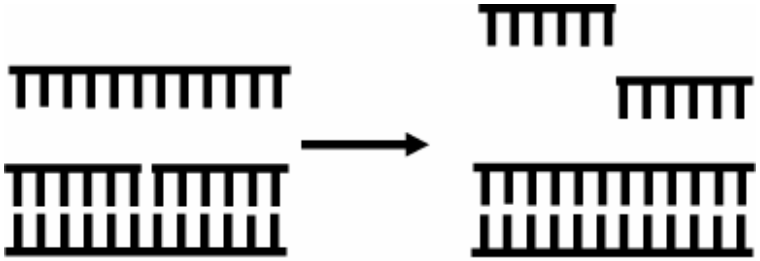
Driven forward by increase in configurational entropy

Motorized DNA tweezers

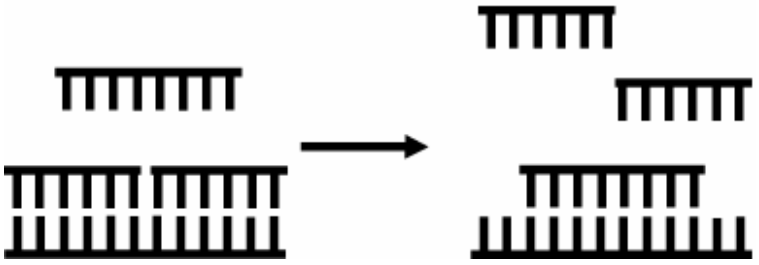


Entropy driven strand displacement

Number of base pairs unchanged



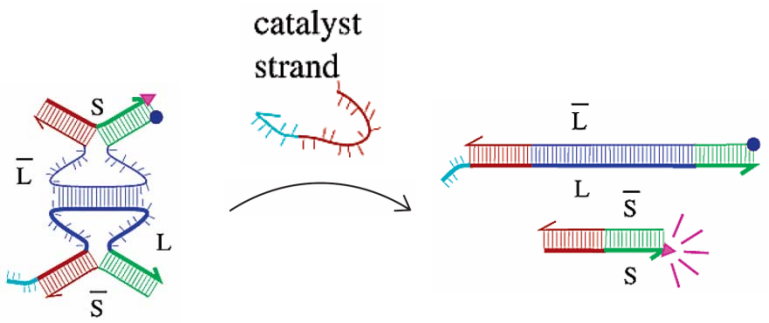
Number of base pairs decreased



Catalytic DNA Systems

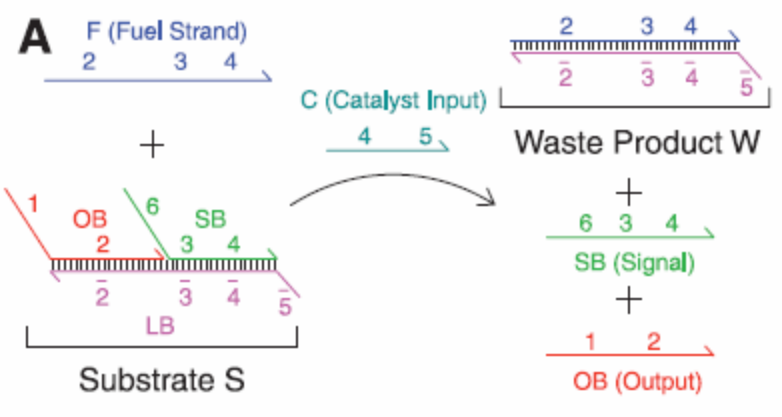
1. Catalytic system powered by increase in the number of bases paired.

   G. Seelig, B. Yurke, and E. Winfree, JACS **129**, 12211 (2006).

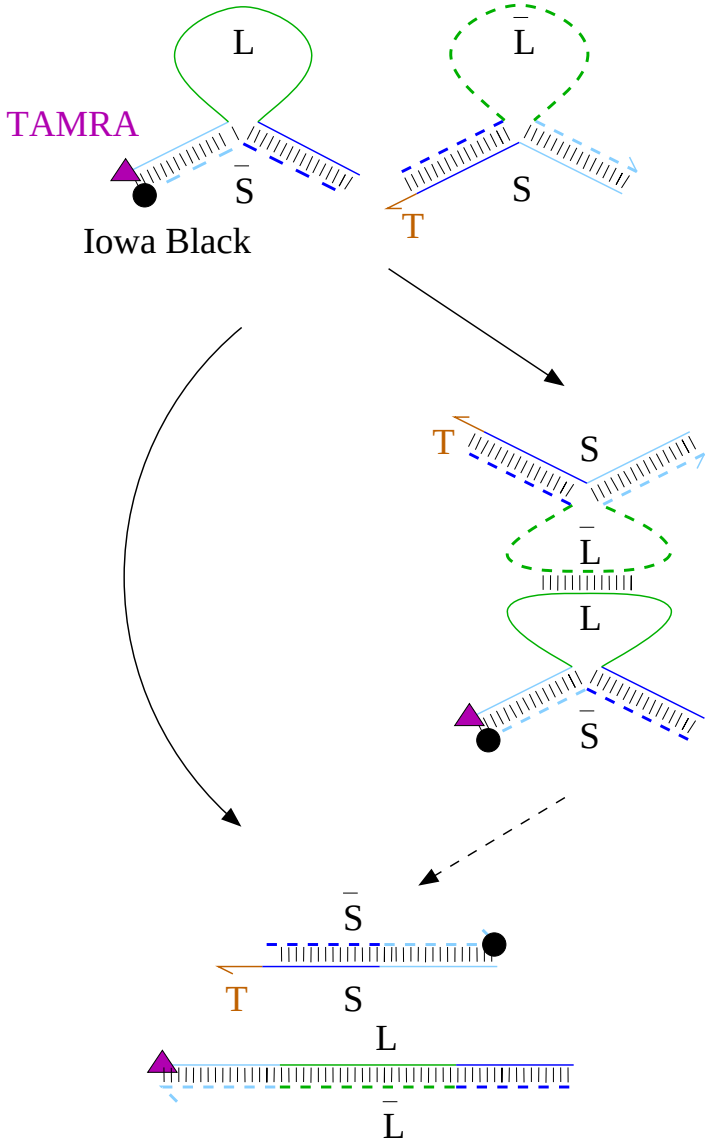


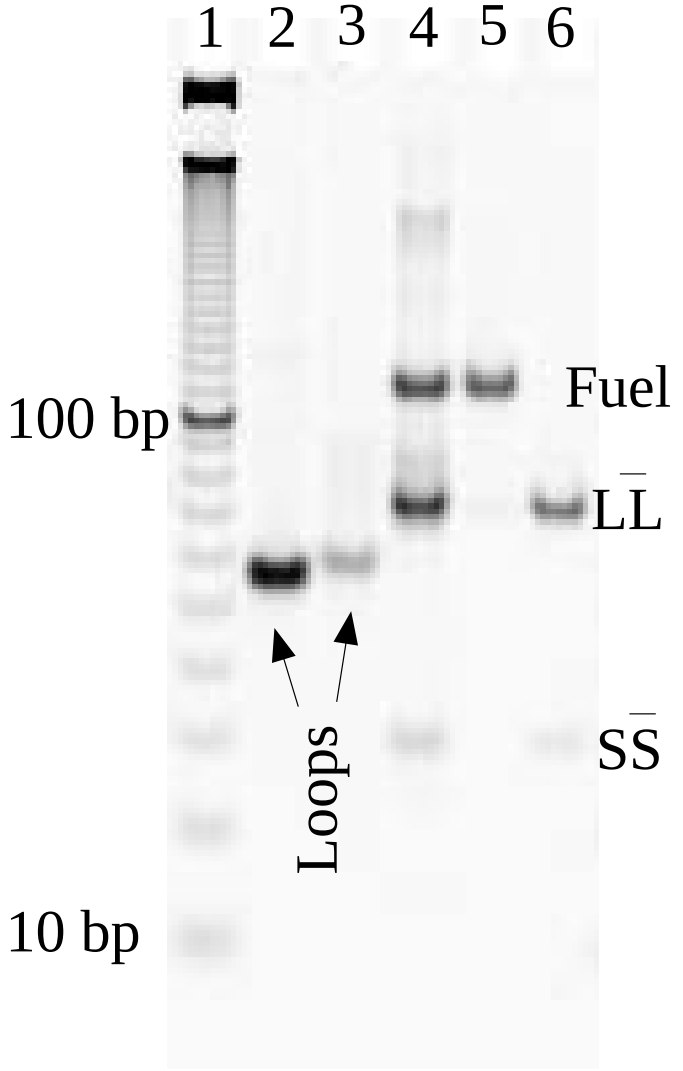
2. Catalytic system entropically driven by increase in the number of DNA strands.

   D. Zhang, A. J. Turberfield, B. Yurke, and E. Winfree, Science **318**, 1121 (2007).



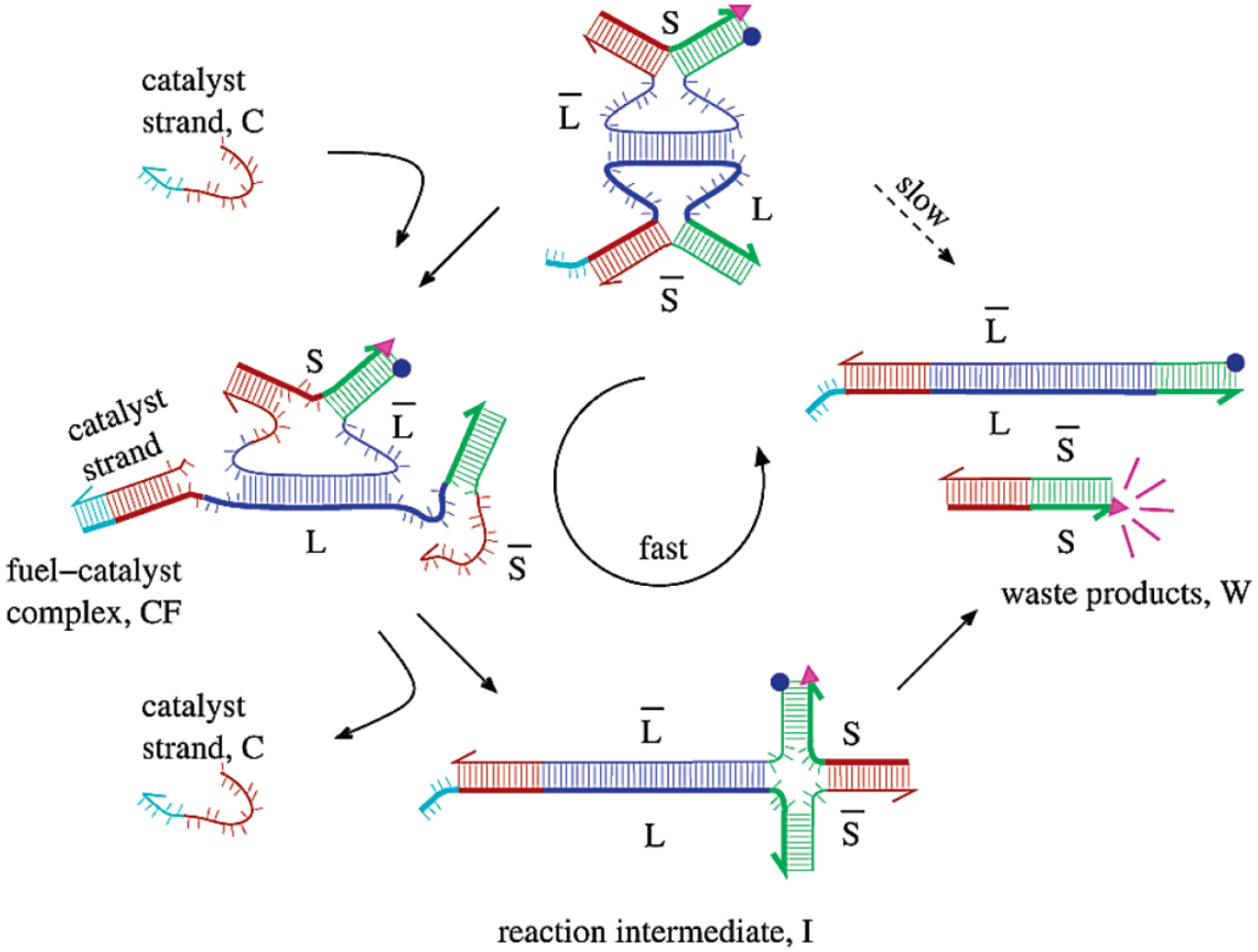
Making a metastable fuel complex



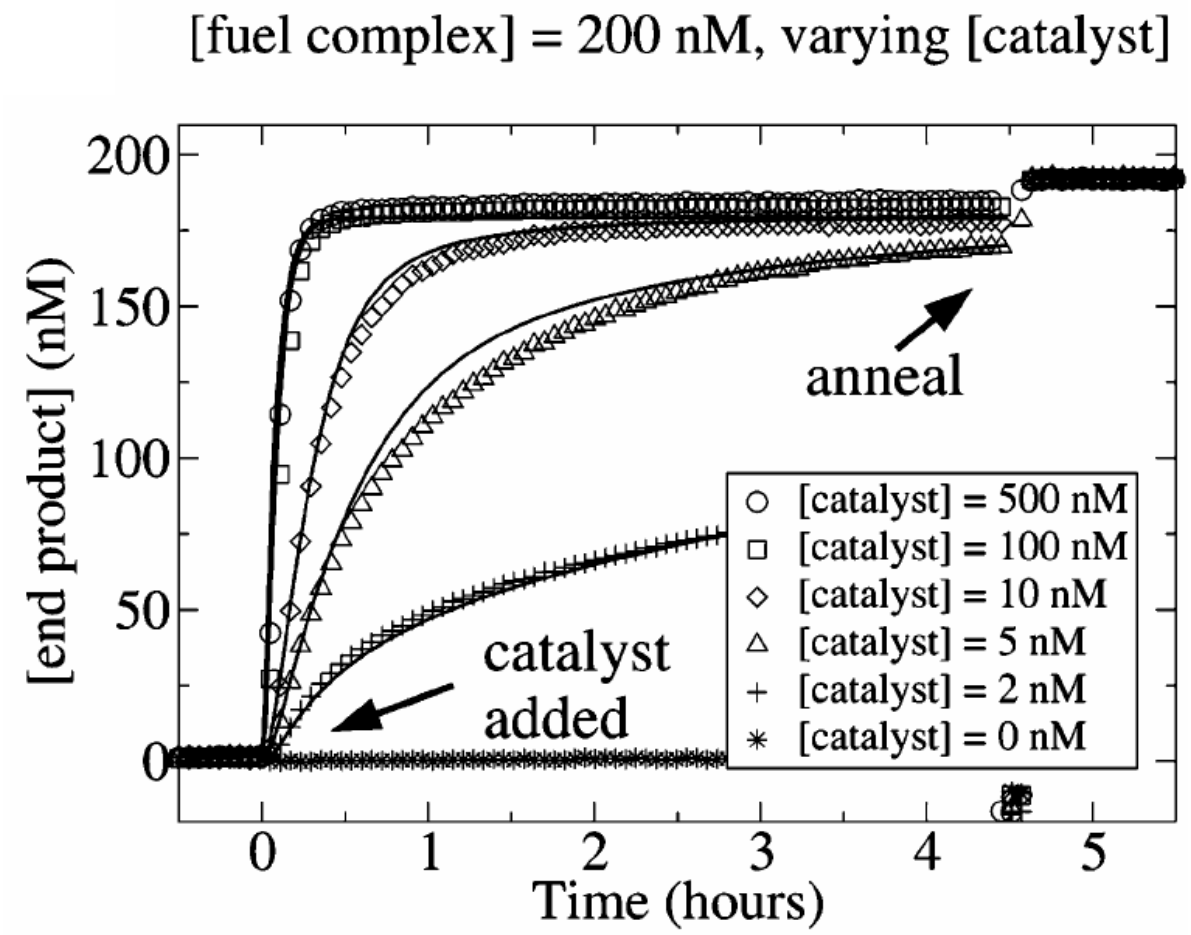


Seelig, et al., JACS 90, 12211 (2006)

Catalytic speedup of fuel-complex decay



Seelig, et al., JACS 90, 12211 (2006)

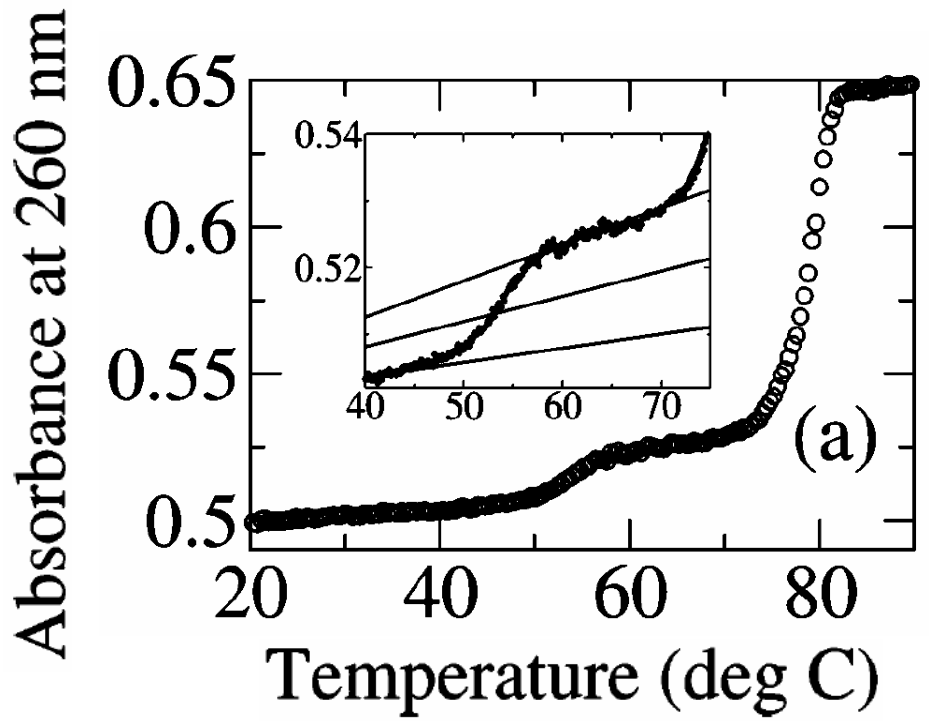


Catalytic speedup: 5000

Turnover : 40

Seelig, et al., JACS 90, 12211 (2006)

Energy content of the fuel



Free energy change due to the kiss

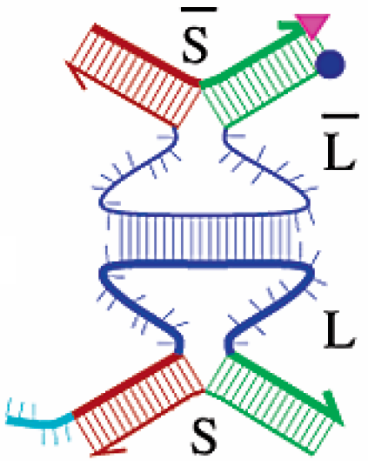
$$\Delta G^{\circ}_{\text{kiss}} = -23 \text{ kcal/mol}$$

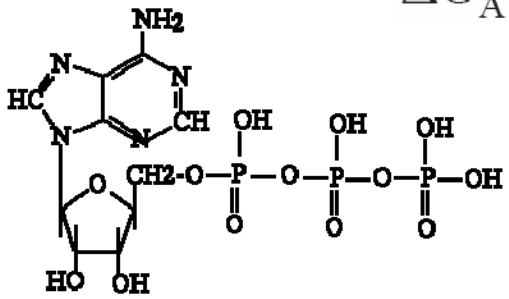
Free energy change do to decay of the fuel complex into waste products

$$\Delta G^{\circ}_{\text{stored}} = -55 \text{ kcal/mol}$$

Free energy change do to decay of ATP into ADP

$$\Delta G^{\circ}_{\text{ATP}} = -7.3 \text{ kcal/mol}$$

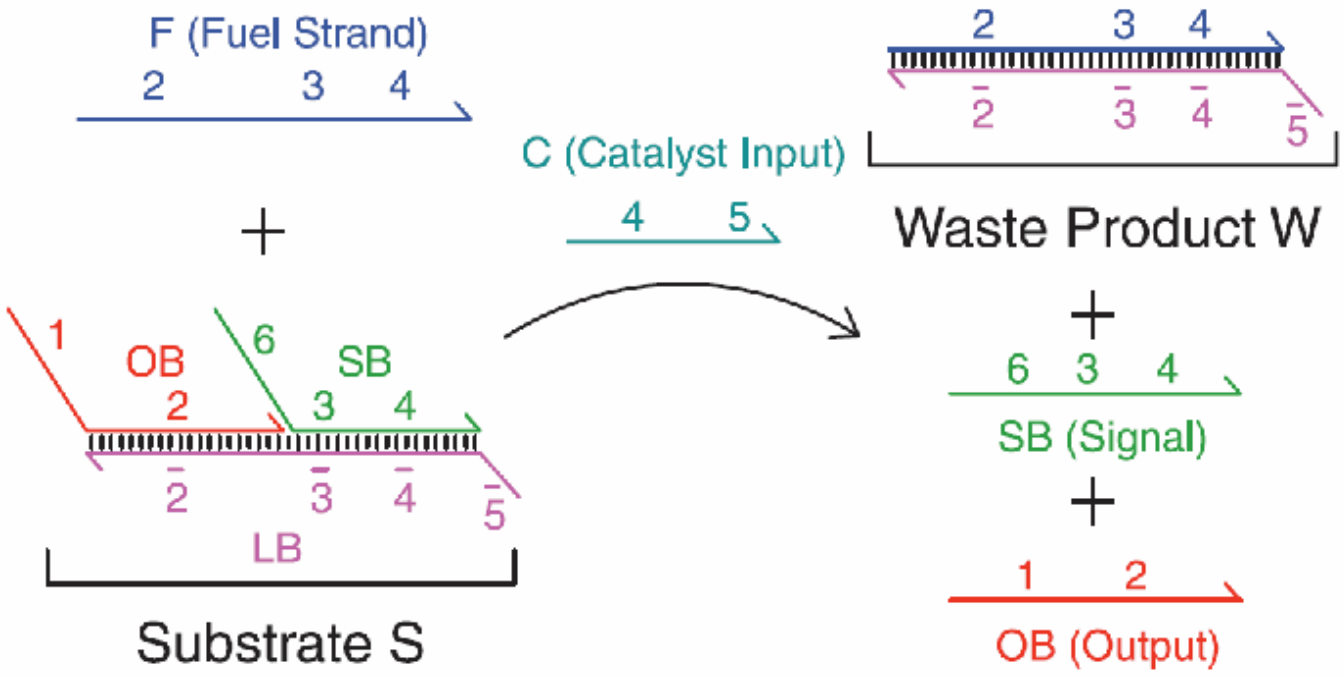




adenosine triphosphate (ATP)

Seelig, et al., JACS 90, 12211 (2006)

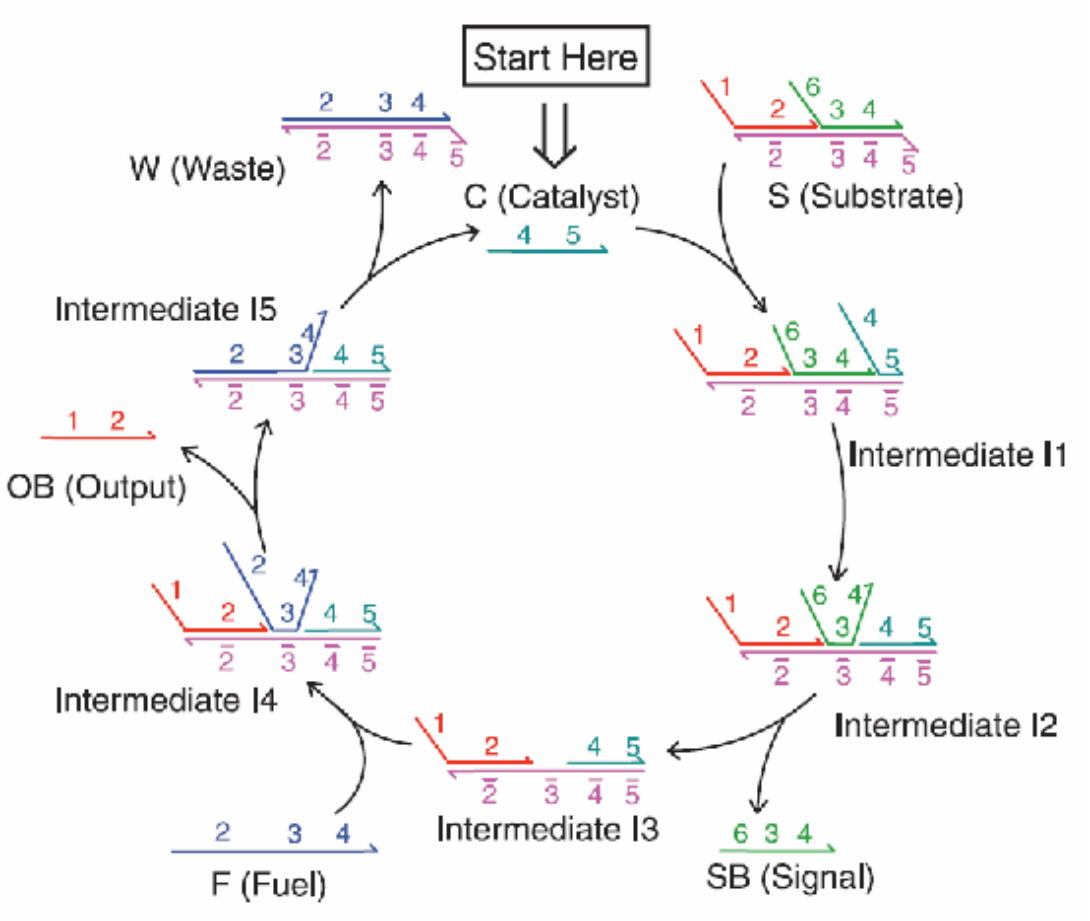
Entropy drive catalyst



D. Zhang, A. J. Turberfield, B. Yurke, and E. Winfree, Science **318**, 1121 (2007).

Entropy drive catalyst

A

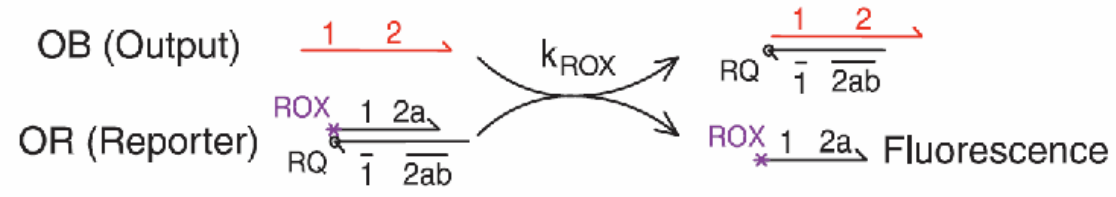


Zhang, et al., Science **318**, 1121 (2007).

Catalytic cycle

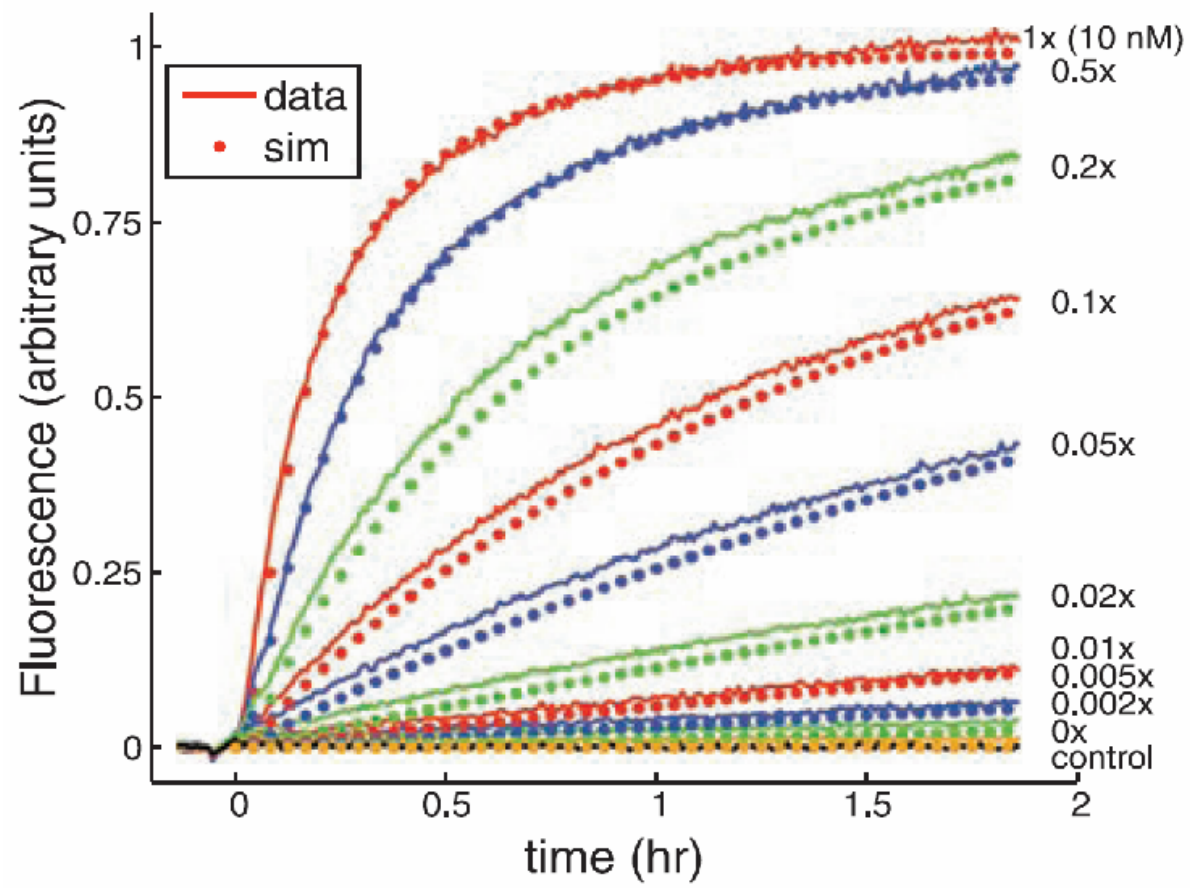
Domain 3 is four bases long.

B



Readout scheme

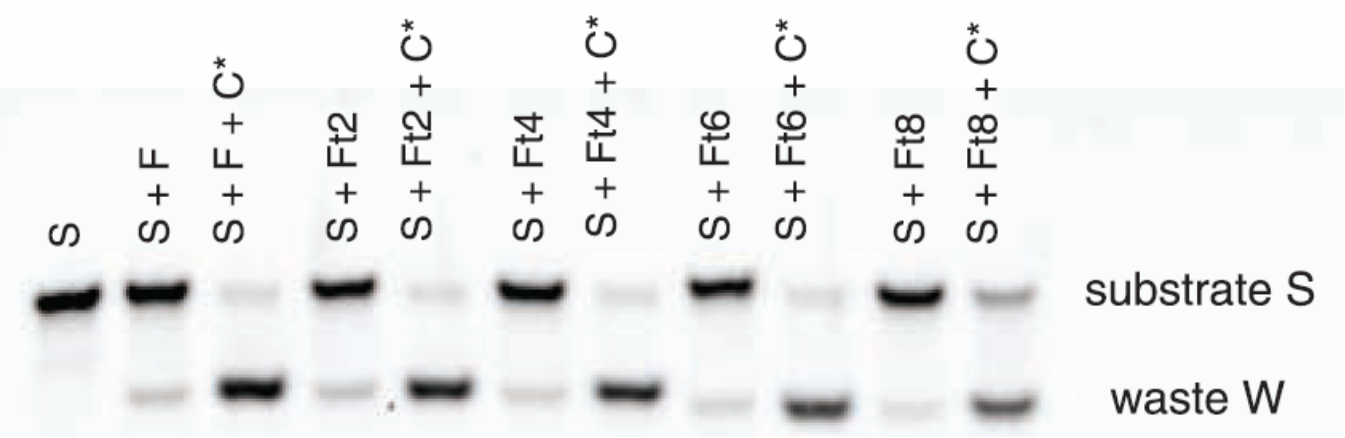
Entropy driven catalyst

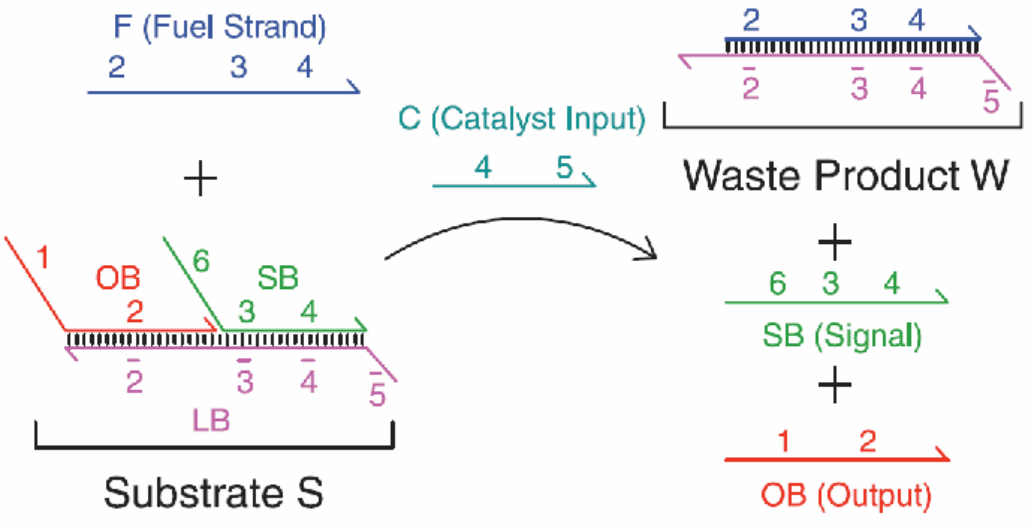


Catalytic speedup: 1.9 X 10^4

Zhang, et al., Science **318**, 1121 (2007).

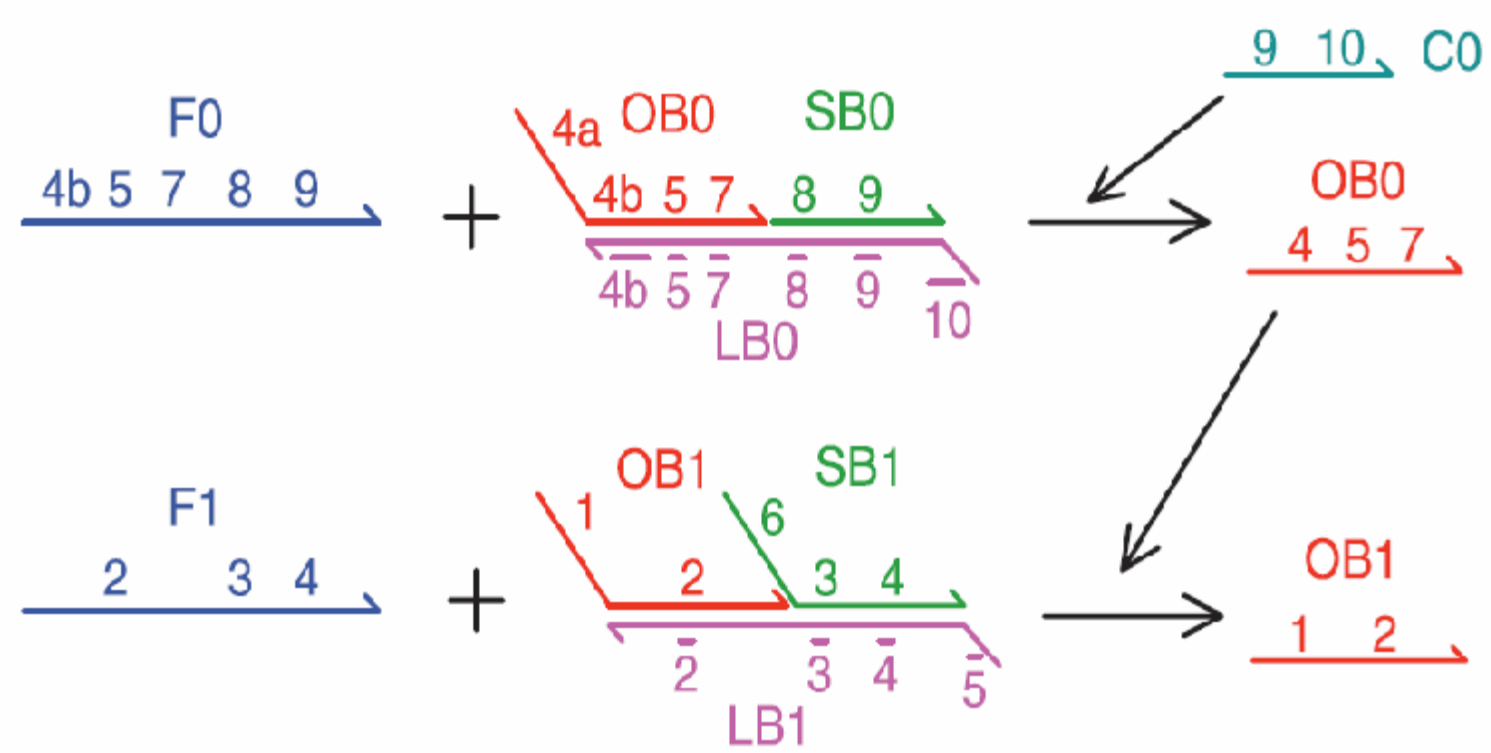
Using entropy to go uphill energetically





Zhang, et al., Science **318**, 1121 (2007).

A catalytic cascade



[C0] is constant with time

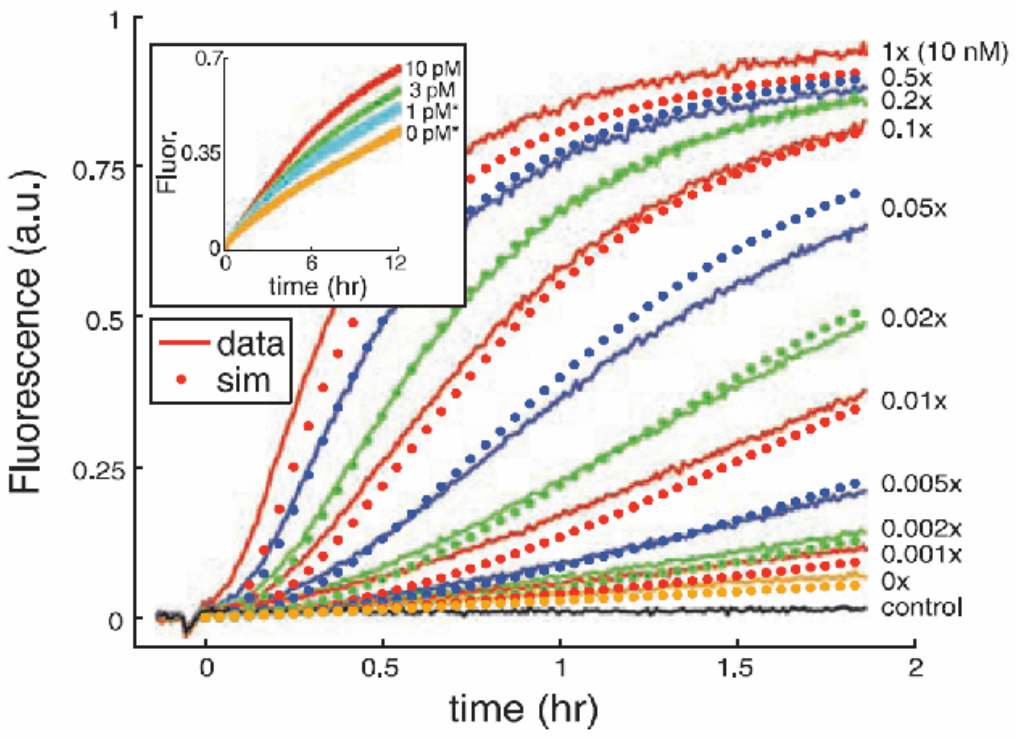
For short times

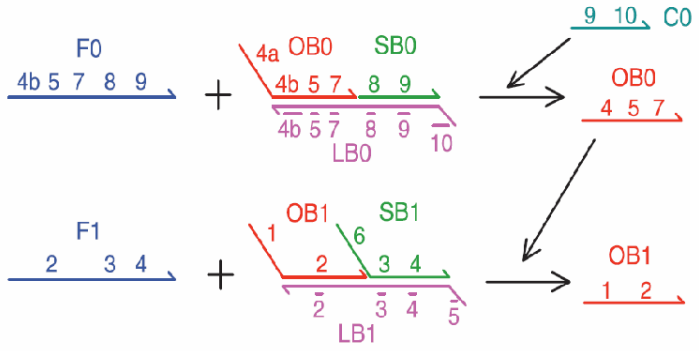
[OB0] is proportional to *t*

[0B1] grows as t^2

Zhang, et al., Science **318**, 1121 (2007).

A catalytic cascade





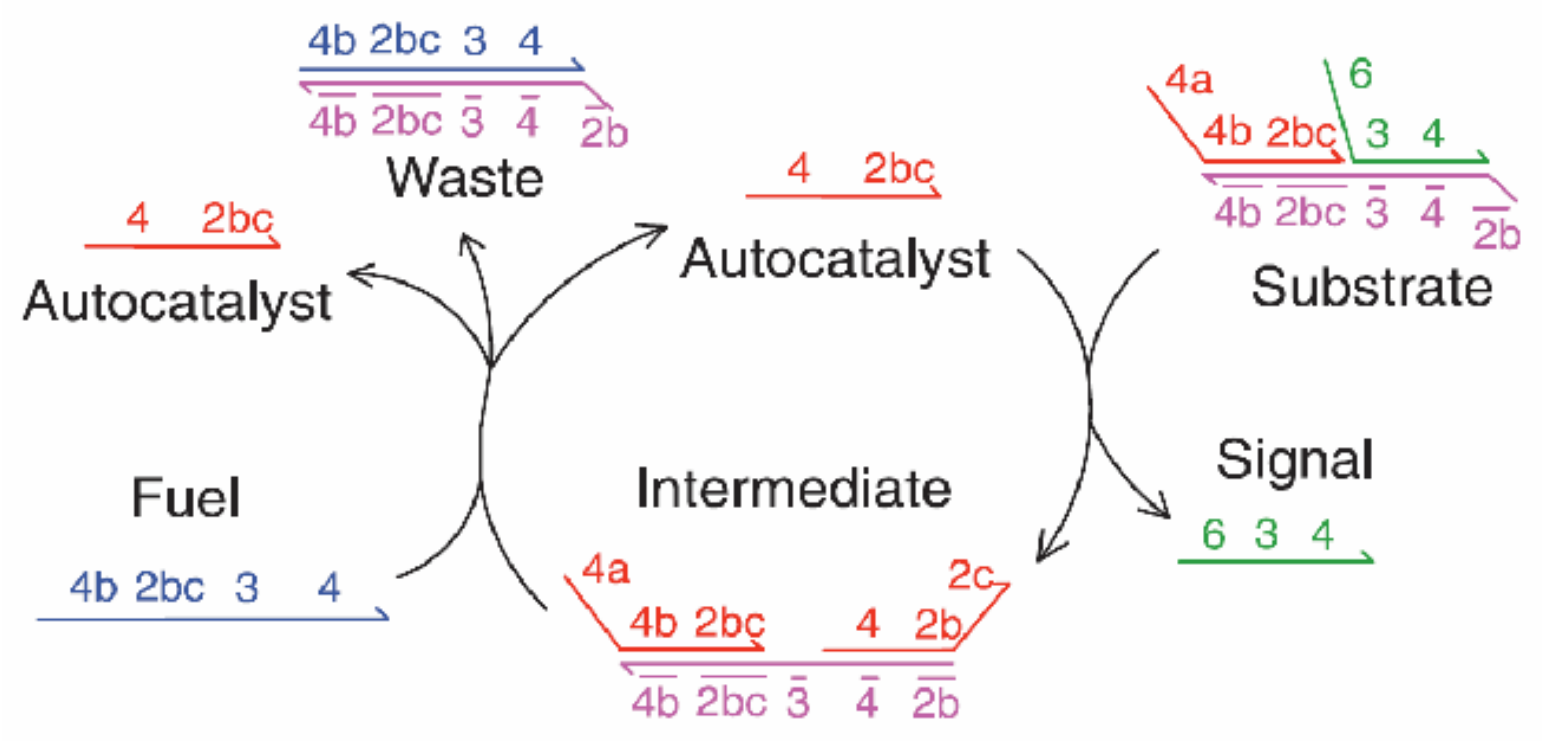
After 12 hours we can reliably distinguish between 0 pM and 1 pM of catalyst. 1pM of catalyst generated 900 pM of reporter.

This is 900 fold amplification.

1 pM corresponds to about one molecule per eukaryotic cell.

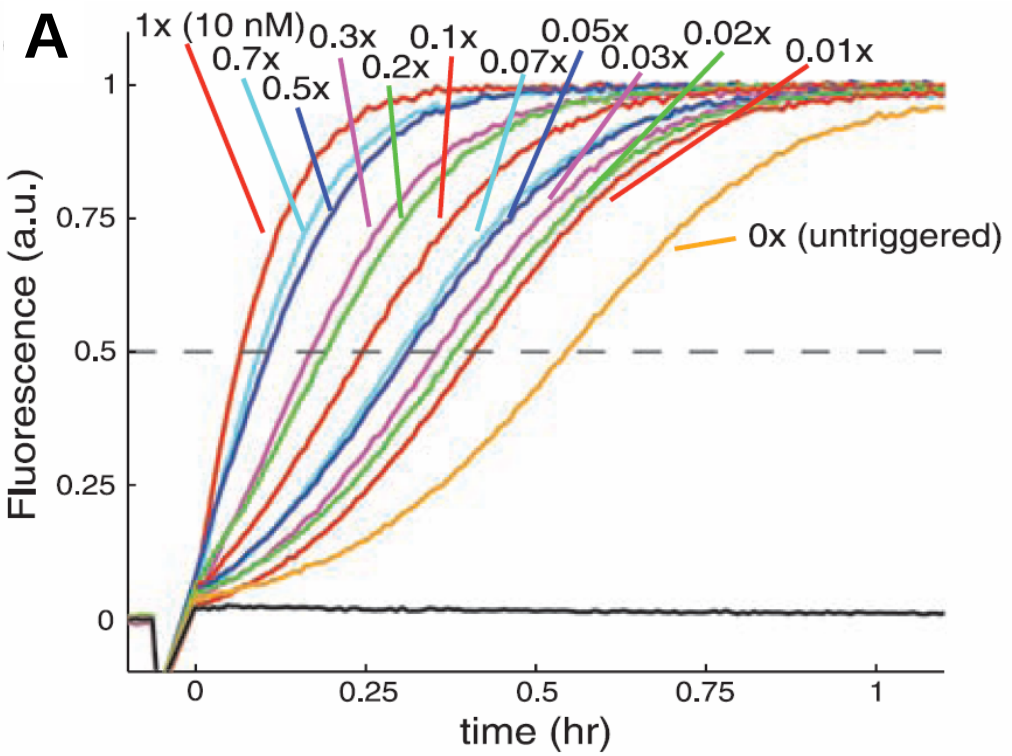
Zhang, et al., Science **318**, 1121 (2007).

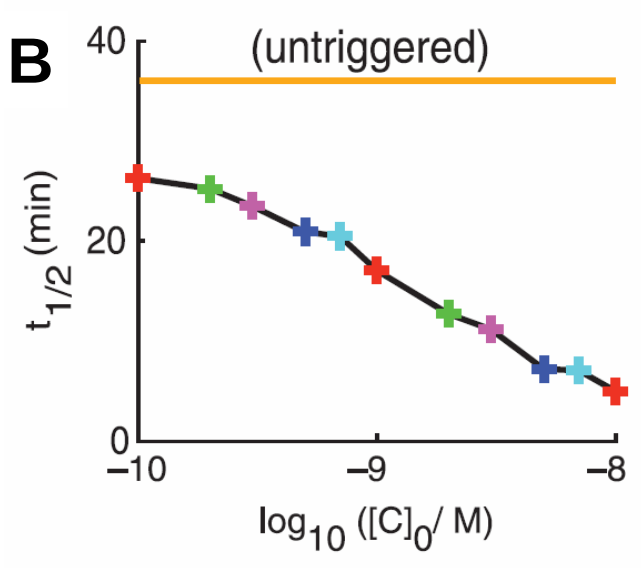
An autocatalytic system



Zhang, et al., Science **318**, 1121 (2007).

Exponential growth with saturation





Zhang, et al., Science **318**, 1121 (2007).

Conclusions

Entropy driven reactions provide a powerfull way to engineer DNA reaction networks.

Catalytic DNA systems have been devised which:

1.exhibit motor activity

SJ Green, J Bath, AJ Turberfield, PRL **101**, 238101 (2008).

2.function similar to biological signaling cascades.

3.exhibit autocatalytic behavior.

Future challenges

1. Make better autonomous DNA-based motor systems.
2. Make chemical amplifiers that would be commercially useful.
3. Make autocatalytic systems that can transmit some sort of genetic information.