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

Toehold mediated strand displacement

Entropy driven strand displacement

Driven forward by increase in the number of base pairs

Driven forward by increase in the number of base pairs

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.
   

2. Catalytic system entropically driven by increase in the number of DNA strands.
   
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
\[ \Delta G_{\text{kiss}}^\circ = -23 \text{ kcal/mol} \]

Free energy change due to decay of the fuel complex into waste products
\[ \Delta G_{\text{stored}}^\circ = -55 \text{ kcal/mol} \]

Free energy change due to decay of ATP into ADP
\[ \Delta G_{\text{ATP}}^\circ = -7.3 \text{ kcal/mol} \]

Seelig, et al., JACS 90, 12211 (2006)
Entropy drive catalyst

Entropy drive catalyst


Catalytic cycle

Domain 3 is four bases long.

Readout scheme
Entropy driven catalyst

Catalytic speedup: $1.9 \times 10^4$

Using entropy to go uphill energetically

A catalytic cascade

[C0] is constant with time
For short times
[OB0] is proportional to $t$  
[OB1] grows as $t^2$

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

1 pM corresponds to about one molecule per eukaryotic cell.

An autocatalytic system

Exponential growth with saturation

Conclusions

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

Catalytic DNA systems have been devised which:
1. exhibit motor activity
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.