Switchable Catalysis

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Switchable Catalysis: Inspiration from Nature

The synthetic machinery of natural systems makes complex polymers with fine temporal and spatial control.

Example: Actin filament polymerization provides structure and allows cells to move.

Initiation, chain-growth, and cross-linking regulated by >100 accessory proteins.

Switchable Catalysis: Inspiration from Nature

The synthetic machinery of natural systems makes complex polymers with fine temporal and spatial control.

Enzymatic activity modulated through feedback loops and trigger-induced effects to prevent parallel reactions in Nature from interfering with one another:

- Operations must be controlled
- Function must be switchable
- Switching must be reversible
Switchable Catalysis: Inspiration from Nature

**switchable catalysis**

toggling chemical reactivity of a catalyst between multiple distinct states

through application of external stimuli

**basic requirements for switches:**

- bistability: occurrence of 2 forms of molecule that can be interconverted by an external stimulus
- fast response times
- thermal stability
- fatigue resistance

Switchable Catalysis

- switchable catalysis: biological inspiration
- types of switchable external stimuli
  - light
  - pH
  - ion coordination
  - redox switching
  - mechanical forces
Switchable Catalysis

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light is an attractive external regulator: low-cost, ubiquitous, noninvasive, precise control

initiates and regulates complex processes with precision in Nature

(e.g., photosynthesis, vision)

types of photocontrol of catalytic activity

photoswitchable catalysis

photocaged catalysis

photocatalysis

reversible toggling between active and inactive catalytic states

irreversible formation of active catalytic state

transient excited state is reactive


**Light-Gated Catalysis**

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**types of photocontrol of catalytic activity**

**photoswitchable catalysis**

**photocaged catalysis**

**photocatalysis**

**catalytic activity from ground-state species**


**Light-Gated Catalysis**

*a photoswitchable catalyst* involves a catalytically active species that undergoes a reversible photochemical transformation altering its catalytic properties.

### azobenzene/stilbene

\[
\begin{align*}
X = \text{N, CH} \\
hv_1 & \leftrightarrow \text{phenyl ring} \\
hv_2 & \leftrightarrow \text{phenyl ring}
\end{align*}
\]

### diarylethene

\[
\begin{align*}
X = \text{S, NH, O} \\
r \neq \text{H} \\
hv_1 & \leftrightarrow \text{diarylethene} \\
hv_2 & \leftrightarrow \text{diarylethene}
\end{align*}
\]

### spiropyran

\[
\begin{align*}
\text{Me} & \text{Me} \\
\text{Me} & \text{Me} \\
\text{Me} & \text{Me} \\
\text{Me} & \text{Me}
\end{align*}
\]

Light-Gated Catalysis

photoswitchable base catalysis

\[
\begin{align*}
\text{Me} & \text{N} \\
t-\text{Bu} & \text{t-Bu}
\end{align*}
\]

\[
\text{N} \quad \text{O} \quad \text{O} \\
\text{N} \quad \text{N}
\]

\[
\begin{align*}
t-\text{Bu} \quad \text{Me} & \quad \text{N} \\
\text{t-Bu} & \text{t-Bu}
\end{align*}
\]

accessible basic site

basicity of deshielded Z isomer increases by almost an order of magnitude

Light-Gated Catalysis

photoswitchable base catalysis

[Chemical structures and reaction scheme]

photoreversible steric shielding in a small molecule catalyst

$k_z/k_E = 35.5$

**Light-Gated Catalysis**

chiral Cu chelation  
high enantioselectivity

no Cu chelation  
low enantioselectivity

large geometrical change induces change in orientation  
of key sites on catalyst (cooperative effect)
Light-Gated Catalysis

chiral Cu chelation
high enantioselectivity

no Cu chelation
low enantioselectivity


in situ photoinduced ring-opening
first in situ photoswitching of stereoselective catalysis

<table>
<thead>
<tr>
<th>ligand</th>
<th>trans</th>
<th>cis</th>
<th>d.r.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>30</td>
<td>50</td>
<td>55:45</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>5</td>
<td>63:37</td>
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Light-Gated Catalysis

chiral Cu chelation
high enantioselectivity

no Cu chelation
low enantioselectivity

$\text{Cu(II)} (10 \text{ mol\%})$

$\text{enantiomer} + \text{enantiomer}$

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limitation: photoinduced ring-closing inefficient with Cu(I)
only 23% of closed form at stationary state at 313 nm

Light-Gated Catalysis

photoinduced changes in electronic properties to alter catalytic activity

mimic of bioactive form of vitamin B6 (pyridoxal 5’-phosphate, PLP)

proof-of-concept: photoinduced regulation of biomimetic, small molecule cofactors
Light-Gated Catalysis

photoinduced changes in electronic properties to alter catalytic activity

mimic of bioactive form of vitamin B6 (pyridoxal 5’-phosphate, PLP)

proof-of-concept: photoinduced regulation of biomimetic, small molecule cofactors

PLP

enzyme cofactor responsible for amino acid metabolism

Light-Gated Catalysis

photoinduced changes in electronic properties to alter catalytic activity

catalytic activity for racemization of L-alanine dependent on electronic connectivity between functional groups

H/D-exchange to monitor catalytic racemization

Light-Gated Catalysis

*photoinduced changes in electronic properties to alter catalytic activity*

![Diagram showing the transformation of a catalyst under UV and visible light, with conversion data.](image)

*after 140 h at 40 °C:*
- 30% conversion with ring-closed catalyst
- < 3% conversion with ring-opened catalyst

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Transient excited state is reactive

catalytic activity from ground-state species

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Photocontrolled Living Radical Polymerization

light used to reversibly activate/deactivate living radical polymerization

- why light? high degree of temporal control over chain growth
- highly responsive external control

\[
{\text{Ir}^{\text{III}}} = \text{fac-}[\text{Ir}(ppy)_3]
\]

in absence of light, no excited state Ir polymerization rests in bromo-capped dormant state
reactivation upon reexposure to light

\[
\begin{align*}
\text{EtO} & \text{Br} \quad \text{MeO} & \text{Me} \quad \text{EtO} & \text{Ph} \\
\text{Ph} \quad \text{Me} \quad \text{CO}_2\text{Me} \\
\text{initiator} & \text{MMA monomer} & \text{bromo-terminated} & \text{chain end}
\end{align*}
\]

Photocontrolled Living Radical Polymerization

light used to reversibly activate/deactivate living radical polymerization

- polymerization stops immediately without light
- existing chain ends reactivated
- no new chain ends initiated during polymerization

Photocontrolled Living Radical Polymerization

Light used to reversibly activate/deactivate living radical polymerization

\[ \ln\left(\frac{[M_0]}{[M_t]}\right) \text{ vs. time of light exposure} \]

Linear relationship between \( M_n \) and conversion

- Polymerization stops immediately without light
- Existing chain ends reactivated
- No new chain ends initiated during polymerization

Photocontrolled Living Radical Polymerization

light used to reversibly activate/deactivate living radical polymerization

- a living polymerization should give efficient block copolymer formation

\[
\begin{align*}
\text{EtO} & \quad \text{O} & \quad \text{Br} \\
\text{MeO} & \quad \text{C} & \quad \text{Me} \\
\text{Ph} & \quad \text{Ir} & \quad \text{III} & \quad \text{(0.005 mol%)} & \quad \text{50 W lamp, DMF, rt} \\
\text{EtO} & \quad \text{O} & \quad \text{Ph} & \quad \text{Me} & \quad \text{CO}_2\text{Me} \\
\text{Me} & \quad \text{Ir} & \quad \text{III} & \quad \text{(0.01 mol%)} & \quad \text{50 W lamp, DMF, rt} \\
\text{EtO} & \quad \text{O} & \quad \text{Ph} & \quad \text{CO}_2\text{Me} & \quad \text{CO}_2\text{Bn} \\
\text{Me} & \quad \text{Br} & \quad \text{m} & \quad \text{n} & \quad \text{M}_W/M_n = 1.28 \\
\text{Me} & \quad \text{CO}_2\text{Me} & \quad \text{CO}_2\text{Bn} & \quad \text{BnO} & \quad \text{Me} & \quad \text{“macroinitiator”}
\end{align*}
\]

- efficient block copolymer formation - LRP
- little to no starting macroinitiator
- minimal termination occurring during polymerization

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pH-Driven Switching

Chemically driven processes based on changes in pH common in both Nature and molecular machines.

In catalysis, pH-switching can modify catalyst solubility.

Catalyst removal after metathesis can be challenging. After protonation, efficient removal of Ru catalyst by filtration.

Redox Switching

control of oxidation state of redox-active ligands to mediate catalytic activity
Redox Switching

control of oxidation state of redox-active ligands to mediate catalytic activity

\[ \text{Fe(t-Bu)O}_{i-Pr} \underset{\text{rapid}}{\overset{\text{slow}}{\rightleftharpoons}} \text{Fe(t-Bu)O}_{i-Pr} \]

\[ \text{MeO} \overset{-2e^-}{\longrightarrow} \overset{+2e^-}{\longrightarrow} \text{MeO} \]

\[ k_{\text{red}}/k_{\text{ox}} = \sim 30 \]

- lactide polymerization known to be slow for e-deficient Ti^{IV}-salen catalysts

Redox Switching

control of oxidation state of redox-active ligands to mediate catalytic activity

[Chemical structures and equations]

reversible nature of redox event demonstrates switching effect

before oxidation: $k_{app} = 4.73 \times 10^{-6} \text{ s}^{-1}$

after $(\text{Cp}^*)_2\text{Fe}$ added: $k_{app} = 4.98 \times 10^{-6} \text{ s}^{-1}$

$k_{app} =$ rate of propagation

Redox Switching

Control of oxidation state of redox-active ligands to mediate catalytic activity

Can redox-switching be used to make micro-block copolymers?

Reversible nature of redox event demonstrates switching effect

Before oxidation: $k_{\text{app}} = 4.73 \times 10^{-6} \text{ s}^{-1}$

After $(\text{Cp}^*)_2\text{Fe}$ added: $k_{\text{app}} = 4.98 \times 10^{-6} \text{ s}^{-1}$

$k_{\text{app}} = \text{rate of propagation}$

Redox Switching

block copolymer synthesis via redox switching of ligands

Redox Switching

change in oxidation state changes binding profile of catalyst

Redox Switching

change in oxidation state changes binding profile of catalyst

minimal change in rate of reaction before/after changing oxidation state of Fe

Redox Switching

\[ \text{in situ redox-switching to achieve a block copolymer} \]

in situ redox-switching to achieve a block copolymer

- ox. Zr complex did not polymerize caprolactone in mixed monomer pool
- more Lewis acidic Zr = increases bond strengths of all intermediates for ox. compound

Electrochemically Mediated Atom Transfer Radical Polymerization

redox control of activity of metal catalyst

\[ E_{1/2} = -0.40 \text{ V vs Ag/Ag}^+ \] cathodic current

\[ E_{1/2} = -0.69 \text{ V vs Ag/Ag}^+ \] anodic current

- in absence of potential, equilibrium favors starting materials

- extent of reduction dictated by applied potential \((E_{app})\)

- shifting \(E_{app}\) to more positive values deactivates polymerization

**Electrochemically Mediated Atom Transfer Radical Polymerization**

*Redox control of activity of metal catalyst*

\[
\text{initiation} \\
\begin{align*}
P_n\text{--Br} & \quad + \quad \text{Cu}^+X(L) & \quad \xrightarrow{k_a} & \quad R' & \quad + \quad \text{Cu}^{II}X(L) \\
P_n\text{--X} & \quad + \quad \text{Cu}^+X(L) & \quad \xrightarrow{k_d} & \quad \text{P}^* & \quad + \quad \text{Cu}^{II}X(L)
\end{align*}
\]

*Equilibrium with dormant species* \\
M \quad \xrightarrow{k_d} \quad M

ATRP depends on active/dormant equilibrium between (lower oxidation state) activators and alkyl halides (P_n\text{--Br}) and between (higher oxidation state) deactivators and radicals (P_n^*)

Electrochemically Mediated Atom Transfer Radical Polymerization

Redox control of activity of metal catalyst

\[
P_{n-Br} + Cu^I X(L) \rightleftharpoons \text{initiation} \quad R' + Cu^{II} X(L) \\
P_{n-X} + Cu^I X(L) \rightleftharpoons \text{equilibrium with dormant species} \quad \rightarrow \quad P^* + Cu^{II} X(L)
\]

\[K_{ATRP} = \frac{k_a}{k_{da}}\]

- Concerted atom transfer mechanism via inner-sphere electron transfer
- Favoring dormant state mediates polymerization, allowing for simultaneous growth of each polymer chain
- Excess reducing agent used to regenerate Cu\textsuperscript{I}X activators from Cu\textsuperscript{II}X\textsubscript{2} deactivators (ARGET)

**Electrochemically Mediated Atom Transfer Radical Polymerization**

\[ E_{1/2} = -0.40 \text{ V vs Ag/Ag}^+ \]

- Applying potential of \(-0.69\) V: 80% conversion in 2 h
- Low dispersity at high conversion \((M_w/M_n = 1.06)\)
Electrochemically Mediated Atom Transfer Radical Polymerization

toggling between $E_{1/2} = –0.69$ V and $E_{1/2} = –0.40$ V exhibits responsive on/off switching of polymerization

$E_{1/2} = –0.40$ V vs Ag/Ag$^+$

anodic current

$P_n$–Br $+$ Cu$^{I}$/Br$^-$/Me$_6$TREN $\rightarrow$ Cu$^{II}$/Br$_2$/Me$_6$TREN $+$ $P_n$–Br

$k_a$

$k_{da}$

cathodic current

$E_{1/2} = –0.69$ V vs Ag/Ag$^+$

$e^-$

termination

repetitive stepping of $E_{app}$ acts as an electrochemical switch to modulate Cu oxidation state

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