Mechanical (Machine-like) Catalysis

~ Let's consider a mechanism other than *energy*-dependent catalysis ~

0. Prologue

0-1 Uncatalyzed reaction

a)

Step i

Reactant collision controlled by the:

Collision Frequency (A)

A

B

reactants

transition state

Step ii

Product formation controlled by the:

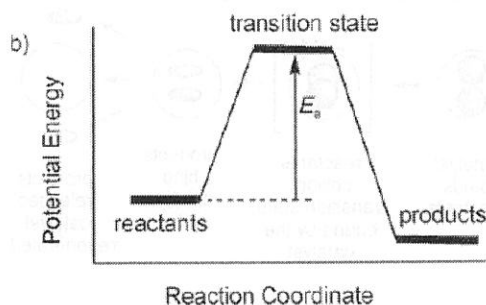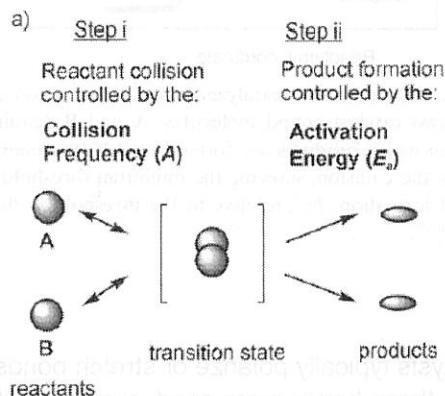**Activation Energy (Eₐ)**

transition state   products

b)

Figure 1. Schematic depiction of an uncatalyzed chemical reaction as: a) a collision between two molecules, A and B, leading to a chemical reaction in which products are formed, and b) the energy profile followed during the collision, showing the minimum threshold energy needed for product formation (termed: the activation energy, E_a).

Based on collision theory, the overall rate of a chemical reaction is given by

<Arrenius equation>

$$k = A \exp\left(\frac{-E_a}{RT}\right)$$

k; reaction rate
A; collision frequency

the proportion of those collisions that are sufficiently energetic to result in product formation

Ea→ 0; every collision brings reaction.

Chemical reactions are controlled by either:

1) the minimum threshold energy that must be overcome during collisions between reactant molecules/atoms (**the activation energy, Eₐ**)

2) the rate at which reactant collisions occur (**the collision frequency, A**) for reactions with low Eₐ.

Reactions 2) are governed by the physical, mechanical interaction of the reactants. Such mechanical processes are unusual, but not unknown in molecular catalysts.

Gerry Swiegers grew up in Port Elizabeth, South Africa, at which University he completed a BSc(Hons) in chemistry. After completing his PhD with Professor Ulli Mueller-Westerhoff at the University of Connecticut, he held academic positions at the Australian National University and the University of Wollongong, Australia. In 1998 he joined the Commonwealth Scientific and Industrial Research Organization (CSIRO) as a research scientist. He is currently Vice-President Research at Datatrace DNA Pty Ltd, a company spun out of his research.

Gerhard F. Swiegers

Dalton Trans., **2009**, 9374.

✱ Ea; large, A; large → **energy-dependent**

Ea; small, A; small → **time-dependent** (diffusion-controlled)

- Most *uncatalyzed* reactions in the *liquid* phase are undoubtedly energy-dependent.
However, time-dependent processes are known. ej.) $H^+ + OH^- \rightarrow H_2O$ (k= ca. 10^{-10} s)

0-2 Catalyzed reaction

Fig. 2

a)

Step i

Reactant collision controlled by the:

Collision Frequency (A)

Step ii

Product formation controlled by the:

Activation Energy (E_a)

catalyst

A   B

reactants

catalyst binds reactants

reactants collide; transition state bound by the catalyst

products bind catalyst

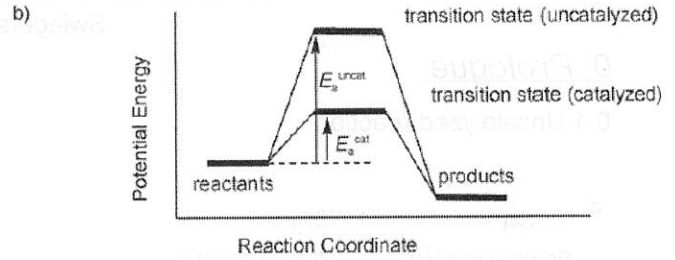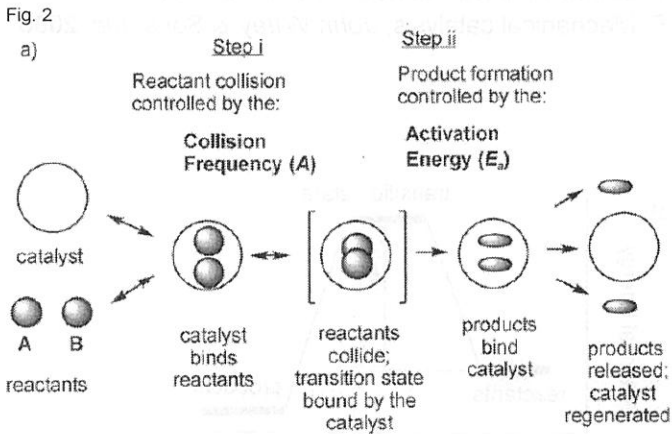products released; catalyst regenerated

b)

Figure 2. Schematic depiction of a catalyzed chemical reaction as: a) a collision between two catalyst-bound molecules, **A** and **B**, leading to a chemical reaction in which products are formed, and b) the energy profile followed during the collision, showing the minimum threshold energy needed for product formation, E_a^{cat}, relative to the threshold in the uncatalyzed reaction, E_a^{uncat}.

a)

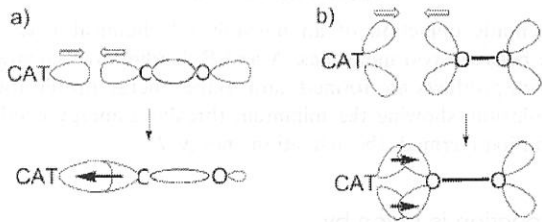CAT ⟶ C ⟶ O≡O

↓

CAT ⟵ C ⟶ O≡O

b)

CAT ⟶ O—O

↓

CAT ⟶ O—O

Figure 3. Reactant activation by a catalyst. Schematic illustrating how a catalyst (CAT) activates a representative reactant (O_2) upon binding, by increasing the O—O bond length in order to facilitate its cleavage. The activation is achieved by either or both of withdrawing electron density from its σ-bonding molecular orbital (left), and increasing electron density in its π*-antibonding orbital (right).

• catalysts typically polarize or stretch bonds, making these bonds more conducive to reaction. (Fig 3)

• catalysts could arrange orientation of reactants. (Fig 2a)

Unlike non-catalyzed reaction

A is dependent on

{
• the rate of reversible catalyst-reactant binding
• the rate at which the catalyst mediate collisions between bound reactants. (via catalyst's *conformational change*)
}

 Compared with uncatalyzed reaction,
the threshold activation energy of the collision (E_a) is low. (Fig 2b)
→ step ii (Fig 2a) is favorable.
→ the reaction rate more likely depends on step i.
→ prone to depend on *catalyst-mediated* collision frequency (A).

✱ The distinction must necessarily exist between energy- and time-dependent actions in molecular catalysis. But it has not been explored in any detail so far.   → Today's contents

~ Contents ~

0. Prologue
    0-1 Uncatalyzed reaction   0-2 Catalyzed reaction

1. Discussion of the nature of mechanical catalysis
    1-1 Reactions governed by their collision frequency are not formally subject to transition-state theory
    1-2 Time-dependent character in *heterogeneous* catalysis
    1-3 Michaelis-Menten kinetics
    1-4 Influence of the strength of the individual catalyst-reactant binding interaction
    1-5 Synergetic effects

2. Perspective

1. Discussion of the nature of mechanical catalysis

1-1 Reactions governed by their collision frequency are not formally subject to transition-state theory

In 1920s, **Hinshelwood-RRK theory** ——— based on collision theory for gas phase reaction
1956 nobel prize

$$A + M \xrightleftharpoons{K} A^* + M \quad \text{(eq. 1)}$$

$$A^* \xrightarrow{k_2} P \quad \text{(eq. 2)}$$

A; a reactant
A*; a reactant in an exited form
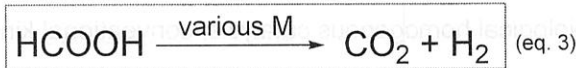M; either a reactant (A) or an added diluent gas molecule

~ two limits ~

1) *high*-pressure limit ;
first order kinetics
rate is governed by the activation energy of the transition state
the system is subject to a *thermodynamic* equilibrium. (eq. 2)

2) *low* pressure limit;
second order kinetics
rate is governed by the frequency of reactant collisions (eq. 1)

In the 1930s, Henry Eyring developed **transition-state theory** by applying quantum mechanics. Eyring had to make the assumption that the reactants, the products, and the transition state were all in *thermodynamic* equilibrium with each other.
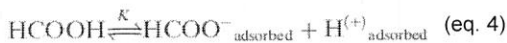
A critical distinction of reactions governed by their collision frequency rather than by their E_a, is that they are not formally subject to *transition-state theory*.

1-2 Time-dependent character in *heterogeneous* catalysis

$$HCOOH \xrightarrow{\text{various M}} CO_2 + H_2 \quad \text{(eq. 3)}$$

A. A. Balandin, *Adv. Catal.* **1958**, 10, 120.

$$HCOOH \xrightleftharpoons{K} HCOO^-_{\text{adsorbed}} + H^{(+)}_{\text{adsorbed}} \quad \text{(eq. 4)}$$

$$H^{(+)}_{\text{adsorbed}} + HCOO^-_{\text{adsorbed}} \xrightarrow{k_2} CO_2 + H_2 \quad \text{(eq. 5)}$$

◆ Sabtier's principle 1912 Nobel Prize winner
an ideal catalyst must bind its reactants but not too strongly.
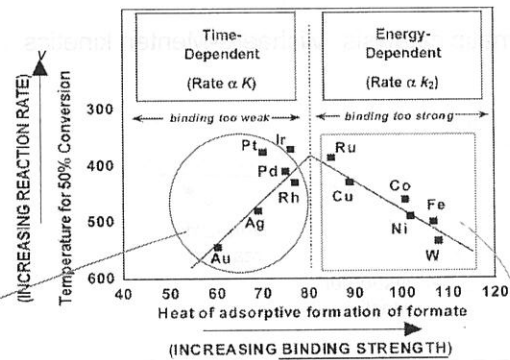

Figure 4. Volcano plot for the decomposition of formic acid by a range of heterogeneous metal catalysts. The constants K and k_2 are those of Equations (2) and (3). The labels "binding too weak" and "binding too strong" are taken from reference [8].

<time-dependent>
• rate increases with binding strength.
(since this increases the likelihood that the reactants will be bound and available for catalyst-mediated collisions)
• eq.4 is rate-limiting (reactant binding and collision).

<energy-dependent>
• rate decreases with binding strength.
• eq. 5 is rate-limiting (overcoming E_a to form products)

◆ Time-dependent character is often observed in heterogeneous catalysts.

✱ when the reactant functionalities bind and release the catalyst rapidly and dynamically, they are attached so briefly that there is little time to collide with each other.

⟹ A mechanical action originates in the physical feature of *dynamic catalyst-reactant binding*.

Summary

1) K   2) τ   3) E_a

catalyst

A   B

reactants

catalyst binds reactants

reactants collide; transition state bound by the catalyst

products bind catalyst
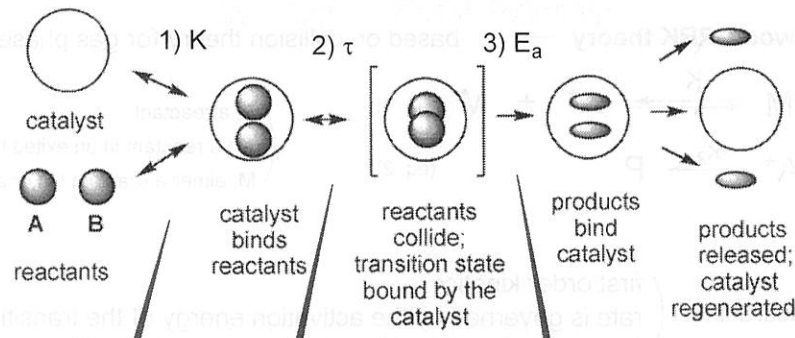
products released; catalyst regenerated

Fig 5.

Time-dependent catalytic actions;
- controlled by reactant binding/ catalyst-mediated collision frequency.
- low pressure limit.
- dynamic catalyst-reactant binding

Energy-dependent catalytic actions;
- controlled by threshold energy (E_a) to be overcome in the transition state.
- high-pressure limit.
- explained by transition-state theory

⇨ Most Enzymatic catalysis acts like here.

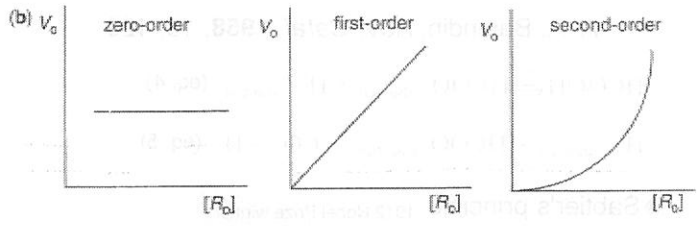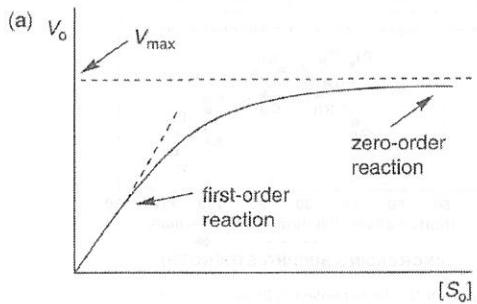⇨ Most nonbiological homogenous catalysis acts like here.

1-3 Michaelis-Menten kinetics

Michaelis-Menten kinetics can be explained by time-dependent catalysis.

$$C + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [CR] \xrightarrow{k_2} C + P \quad \text{(eq. 6)}$$

C; catalyst
R; reactant
P; product
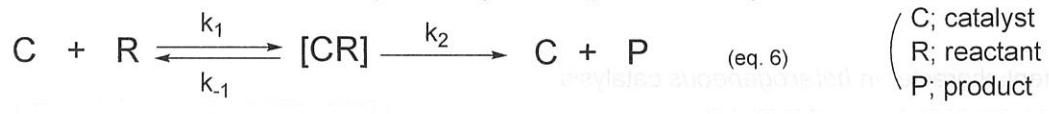
Most Enzymatic catalysis; Michaelis-Menten kinetics

(a) V_0

V_{max}

zero-order reaction

first-order reaction

$[S_0]$

Most nonbiological homogenous catalysis; conventional kinetics

(b) V_0 zero-order V_0 first-order V_0 second-order

$[R_0]$ $[R_0]$ $[R_0]$

rate is determined by
1) equilibrium constant K $K = \dfrac{k_1}{k_{-1}}$
2) the average residence time (τ),
(the reactants is attached and available for catalysis on each occasion of binding) (Fig. 5)

Usually K is large   ($1/K_M \sim 10^{4\pm3}$, $K_M = \dfrac{k_{-1} + k_2}{k_1}$)
↓
residence time τ; small

✱ At any time, most catalytic centers are involved in *receiving or releasing reactants* not in *holding them.*

τ ; an intrinsic and unchanging feature of the system.
the sole and invariant determinant of the rate upon saturation.

rate is determined by k_2, overcoming energy barrier E_a.

an increasing in [R] merely shorten the time between P leaving C and next R attaching C.
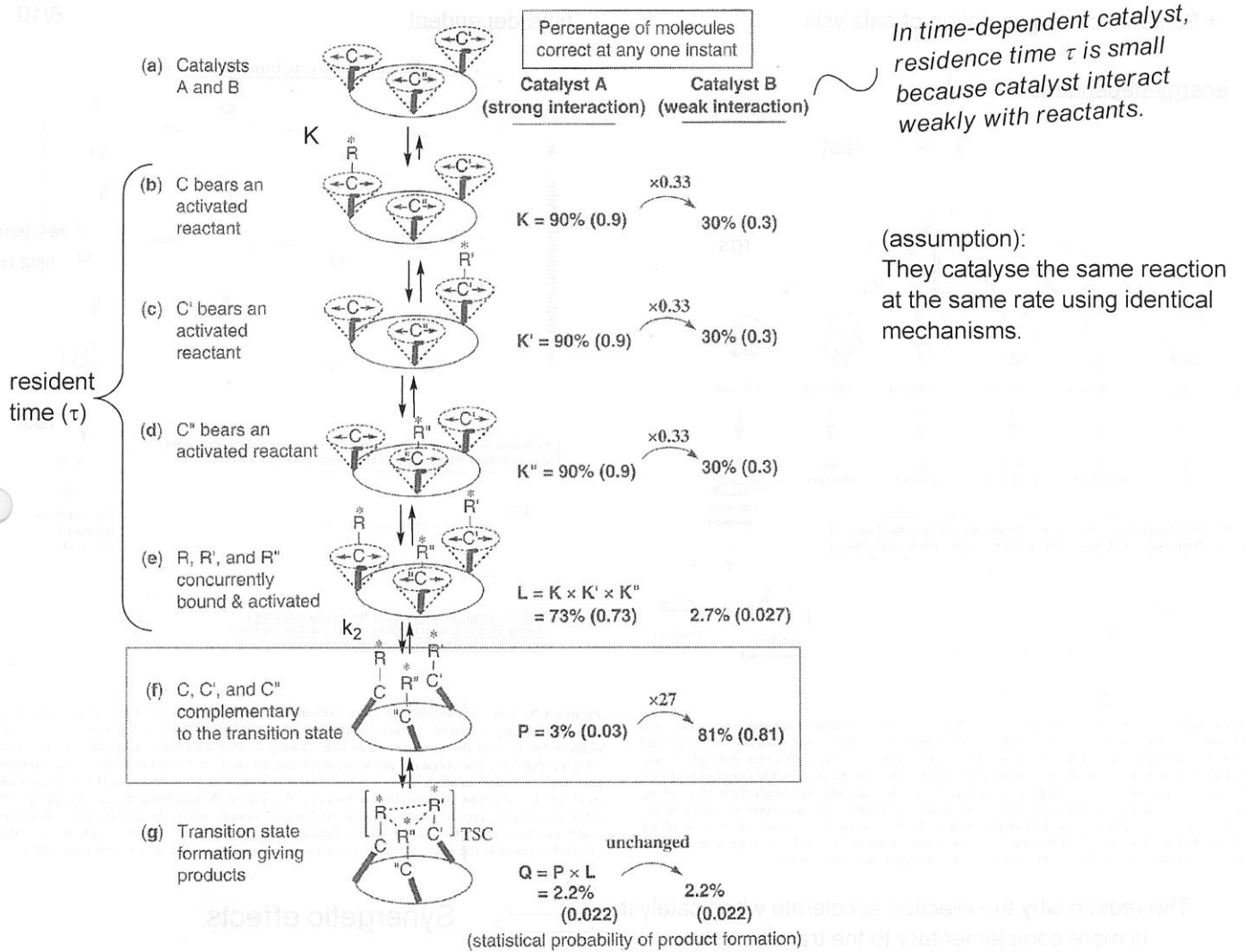↘ 0; then saturated

• saturation occurs when [R] is *absolutely* high.
→ rarely observed.

• saturation occurs when [R] is *relatively* high *to [C]*.
→ often observed.

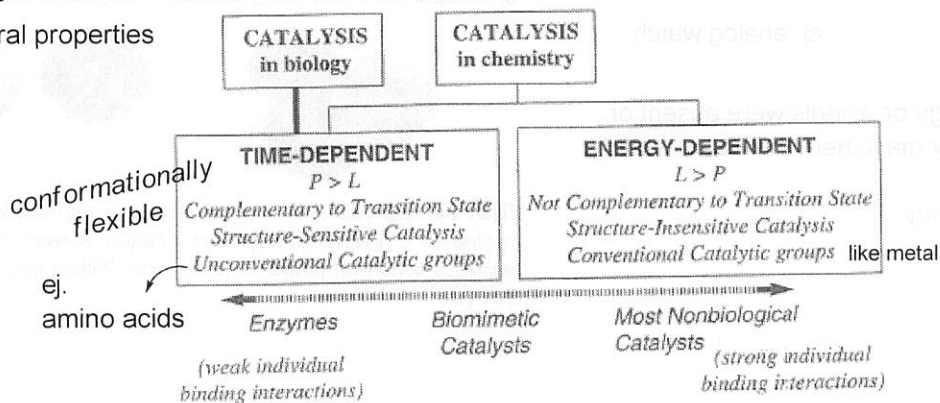♦ saturation kineics is an indication of time-dependence.

In order to illustrate the relationship between collision frequency and energetic efficiency,
Let's consider two hypothetical *homogenous 3-centered* catalysts A and B.

	Percentage of molecules correct at any one instant	
	Catalyst A (strong interaction)	Catalyst B (weak interaction)

(a) Catalysts A and B

In time-dependent catalyst, residence time τ is small because catalyst interact weakly with reactants.

(b) C bears an activated reactant
$\times 0.33$
$K = 90\%\ (0.9)$ → $30\%\ (0.3)$

(assumption):
They catalyse the same reaction at the same rate using identical mechanisms.

(c) C' bears an activated reactant
$\times 0.33$
$K' = 90\%\ (0.9)$ → $30\%\ (0.3)$

resident time (τ)

(d) C" bears an activated reactant
$\times 0.33$
$K'' = 90\%\ (0.9)$ → $30\%\ (0.3)$

(e) R, R', and R" concurrently bound & activated
$L = K \times K' \times K''$
$= 73\%\ (0.73)$ $2.7\%\ (0.027)$

k_2

(f) C, C', and C" complementary to the transition state
$\times 27$
$P = 3\%\ (0.03)$ → $81\%\ (0.81)$

(g) Transition state formation giving products
TSC
unchanged
$Q = P \times L$
$= 2.2\%$ 2.2%
(0.022) (0.022)
(statistical probability of product formation)

Figure 5.4. Schematic determination of the statistical probability of transition state formatic in the three-center catalysts A and B (C, C', C" = catalytic groups; R, R', R" = reactant K–Q = the percentage of molecules that are catalytically optimum).

Summary

as general properties

conformationally flexible

ej. amino acids

CATALYSIS in biology	CATALYSIS in chemistry

TIME-DEPENDENT	ENERGY-DEPENDENT
$P > L$	$L > P$
Complementary to Transition State	Not Complementary to Transition State
Structure-Sensitive Catalysis	Structure-Insensitive Catalysis
Unconventional Catalytic groups	Conventional Catalytic groups like metal

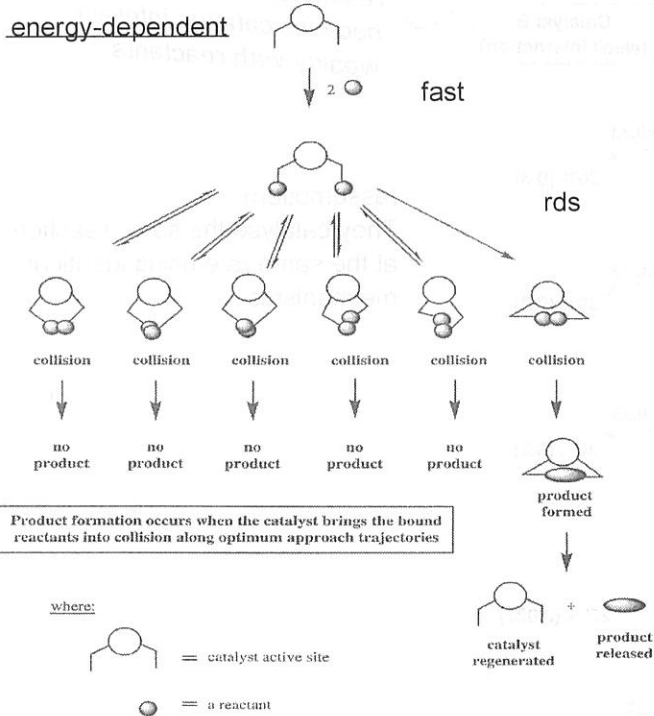| Enzymes	Biomimetic Catalysts	Most Nonbiological Catalysts
(weak individual binding interactions)		*(strong individual binding interactions)*

Figure 5.5. The conceptual overlap of multicentered catalysis in chemistry and biology.
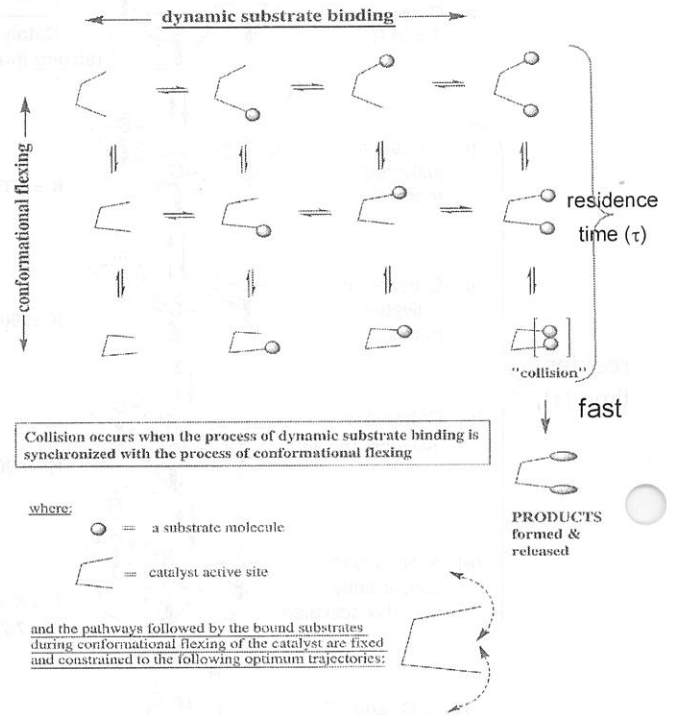
★Schematic representation of catalysis   time-dependent

energy-dependent

Figure 6.2. *Energy-dependent catalysis*: Schematic representation of the catalytic action in a conformationally unconstrained dicentered homogeneous catalyst. The catalyst first binds and holds the two reactants. Then it brings them into collision with each other multiple times. Because it is conformationally unconstrained, these collisions involve a wide variety of relative orientations. In only one set of these orientations do the reactants approach each other along trajectories and pathways that are suitable for reaction. That is, the *activation* provided to the reactants by the catalyst is such that reaction will only occur if the reactants collide along these particular pathways and trajectories. When this happens, the activation provided by the catalyst exceeds the minimum threshold energy and products are formed.

Figure 1.9. *Time-dependent catalysis*: Schematic representation of the two key processes present in many enzymes. Shown on the left, from top to bottom, is the process of *conformational flexing* of the enzyme active site. During conformational flexing, the groups in the enzyme that bind the substrate are repeatedly moved back and forth over the same optimum pathways in space, relative to each other. Shown at the top, from left to right, is the process of *dynamic substrate binding*. In this process, the substrate repeatedly binds and releases the relevant enzyme groups. A successful "collision" occurs when these processes of *conformational flexing* and *dynamic substrate binding* are synchronized, that is, when the substrates are fully bound at the instant that they are brought into physical contact with each other.

| The reason why the reaction accelerate when catalyst is more complementary to the transition state. | ⟹ | Synergetic effects |

1-5 Synergetic effects

When the whole of a system exceeds the simple sum of its constituent parts, the system is said to exhibit synergy.

• Synegy is inherent to many mechanical systems.

                ej. analog watch

- If even one of cogs or wheels were absent or if it was imperfectly machined, the watch would be inoperable.

→ *High convergency*
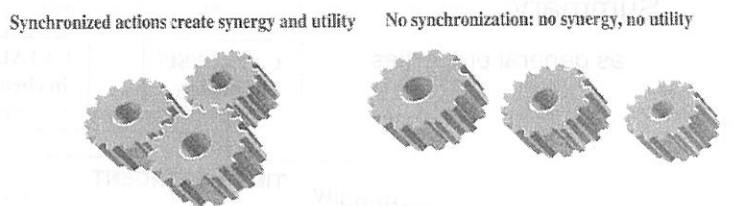
Figure 1.6. *Mechanical systems* are characterized by *synchronization* of actions to yield an outcome that is more than the simple sum of the parts (*synergy*). With such synchronization, mechanical devices can perform astounding feats. Without it, they are just a collection of spare parts.
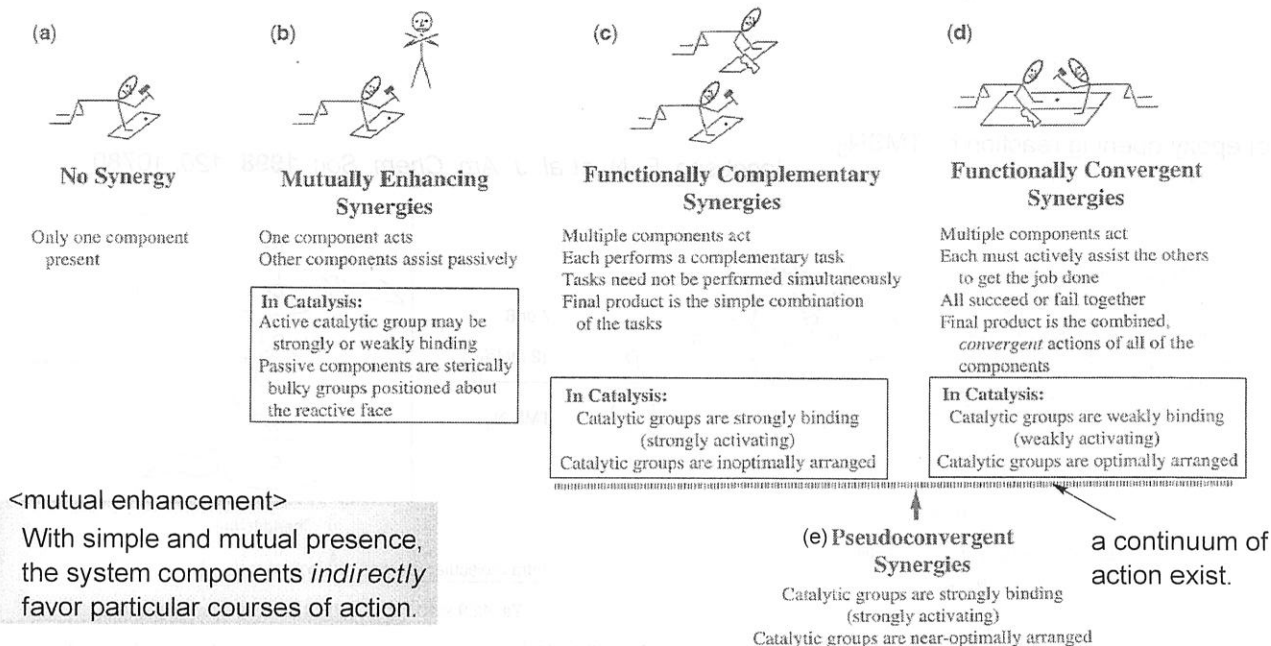
(a)

No Synergy

Only one component
present

(b)

**Mutually Enhancing
Synergies**

One component acts
Other components assist passively

In Catalysis:
Active catalytic group may be
strongly or weakly binding
Passive components are sterically
bulky groups positioned about
the reactive face

(c)

**Functionally Complementary
Synergies**

Multiple components act
Each performs a complementary task
Tasks need not be performed simultaneously
Final product is the simple combination
of the tasks

In Catalysis:
Catalytic groups are strongly binding
(strongly activating)
Catalytic groups are inoptimally arranged

(d)

**Functionally Convergent
Synergies**

Multiple components act
Each must actively assist the others
to get the job done
All succeed or fail together
Final product is the combined,
convergent actions of all of the
components

In Catalysis:
Catalytic groups are weakly binding
(weakly activating)
Catalytic groups are optimally arranged

<mutual enhancement>
With simple and mutual presence,
the system components *indirectly*
favor particular courses of action.

**(e) Pseudoconvergent
Synergies**

Catalytic groups are strongly binding
(strongly activating)
Catalytic groups are near-optimally arranged

a continuum of
action exist.

Figure 8.10. The hierarchy of synergy in catalysis. [Synergy increases in the order (a) to (d)].

<convergence>
the activities undertaken by the
different men converge in a mutually
reinforcing and amplifying way.

Examples

(b): Catalytic propylene polymerization using zirconocene catalyst

Brintzinger, H. H. *et al. Angew. Chem. Int. Ed.* **1995**, *34*, 1143-1170.

where
R = Me, alkyl
MAO = methylaluminoxane
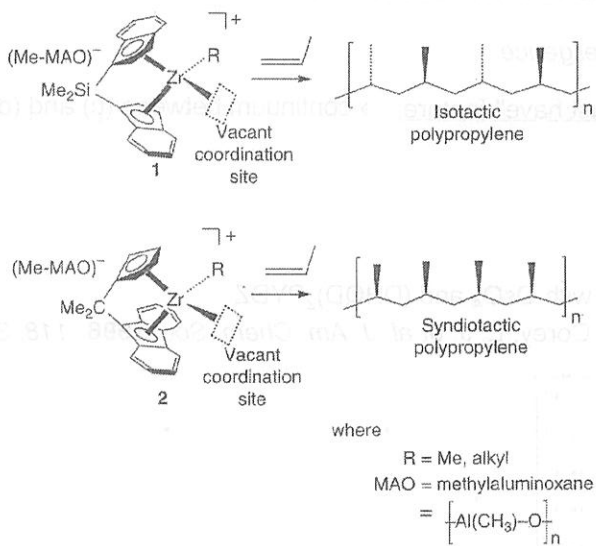$= \left[Al(CH_3)-O \right]_n$

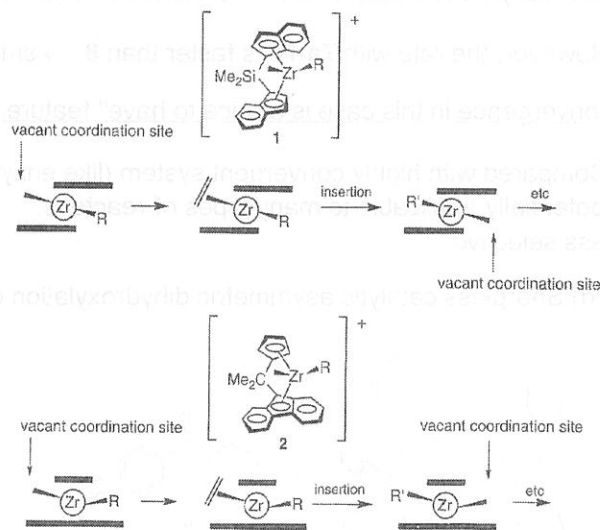Figure 8.2. Catalytic propylene polymerization using zirconocene catalysts.

Figure 8.3. Schematic illustration of the catalytically active face of the Zr ion in 1 and 2
showing the positions of the indenyl and fulvenyl ligands as thick black lines.

- Although indenyl and fluorenyl groups in **1** and **2**, don't participate directly in the catalytic action,
they are significant bystanders to bring the control of the process.

⇒ **mutual enhancement**

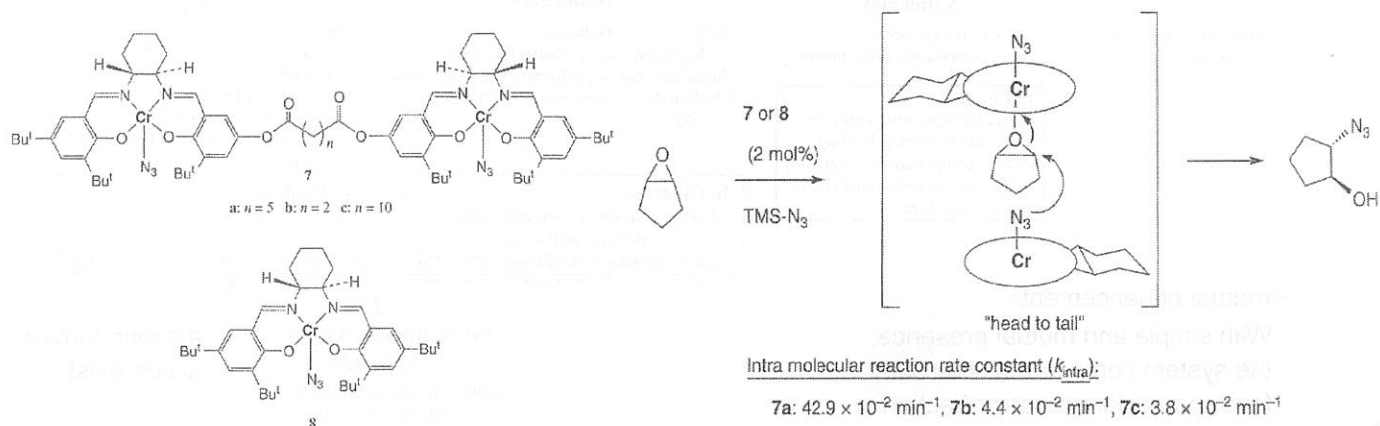- *molecular chaperon* in biology is
also one example.

(c) epoxy opening reaction by TMSN$_3$

Jacobsen, E. N. *et al. J. Am. Chem. Soc.* **1998**, *120*, 10780.

7 or 8
(2 mol%)

TMS-N$_3$

"head to tail"

Intra molecular reaction rate constant (k_{intra}):

7a: 42.9×10^{-2} min^{-1}, **7b**: 4.4×10^{-2} min^{-1}, **7c**: 3.8×10^{-2} min^{-1}

Figure 8.6. *Multicentered homogeneous catalysis.* Functional complementary syner during an asymmetric catalytic ring-opening of an epoxide.

- One Cr ion; bind and activate the *azide*
- the other Cr ion; bind and activate the *epoxide* } complementally activate

When these two tasks are combined, a catalytic effect is achieved.   **functional complementarity**

• There is almost no need for individual catalytic groups to coordinate or synchronize their action, because there is essentially no limitation to the time available to mediate collision between bound reactants.

However, the rate with **7a-7c** is faster than **8**. → small *convergence*

Convergence in this case is a "nice to have" feature, not "must have" feature. → continuum between (c) and (d)

• Compared with highly convergent system (like enzyme)
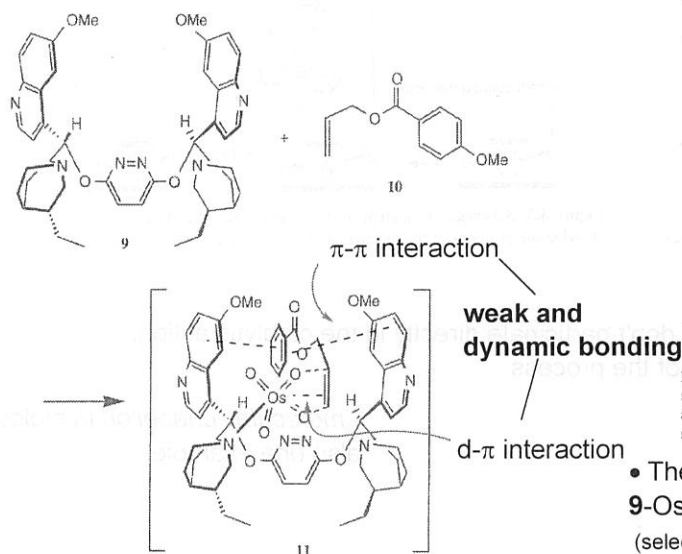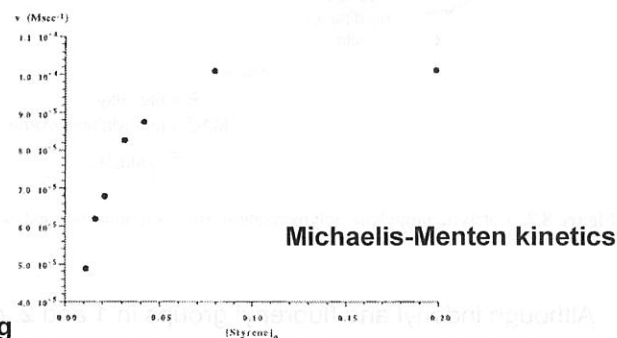+ potentially applicable to many types of reactons.
- less selective

(d) Sharpless catalytic asymmetric dihydroxylation of olefin with OsO$_4$ and (DHQD)$_2$PYDZ

Corey, E. J. *et al. J. Am. Chem. Soc.* **1996**, *118*, 319.

π-π interaction

weak and dynamic bonding

d-π interaction

Michaelis-Menten kinetics

Figure 7. Plot of initial velocity versus initial olefin concentration showing saturation behavior for the (DHQD)$_2$PYDZ·OsO$_4$ catalyzed asymmetric dihydroxylation using 1 mM (DHQD)$_2$PYDZ ligand, 0.5 mM K$_2$OsO$_4$·2H$_2$O in 1:1 *tert*-butyl alcohol-water at 0 °C.

• The enantioselective acceleration occurs. (←the shape of **9**-OsO$_4$ active site can be complementary to the TS.)

(selective acceleration of the pathway leading to the preferred enantiomer)

• Product was obtained in high enantio*selectivity* (98% ee)

Figure 8.8. *Time-dependent, multicentered homogeneous catalysis.* Bis-cinchona alkaloid catalyzed dihydroxylation of olefins.

⟹ **functional convergency**

(e) Cyclodextrin-appended epoxidation catalyst

Breslow, R. *et al. J. Am. Chem. Soc.* **1996**, *118*, 11678.

<competitve experiment>

11 (1 mmol)   10 mol%
0.5 equiv. iodosylbenzeme
adamantane-1-carboxylic acid (5 eq.)

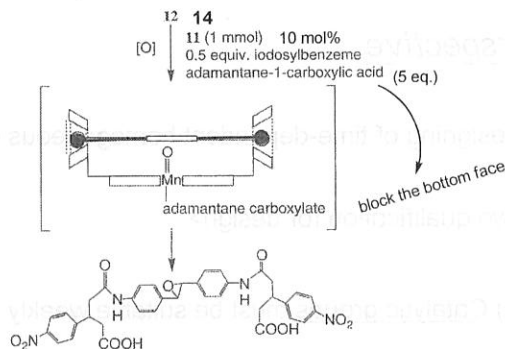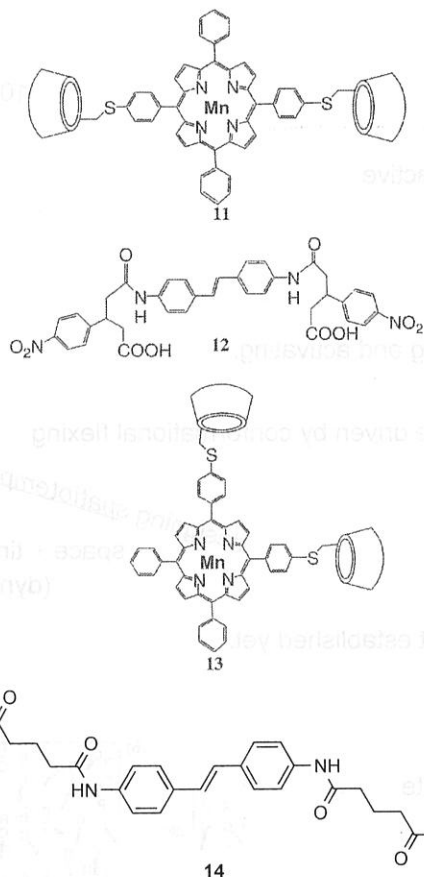block the bottom face

adamantane carboxylate

Figure 8.9. *Pseudo-convergence in a biomimetic catalyst.* Mn porphyrin **11** oxidizes substrate **10** with high, but not perfect, selectivity. Porphyrin **12** shows little selectivity under comparable conditions. Catalyst **11** therefore displays functional convergence on most, but not all, turnovers.

- known as biomimetic catalyst in term of complementary to the TS.

   (although it generally omits dynamic catalyst-reactants interaction)

- **11** does epoxidation of inner olefin in **12** selectively, but not exclusively.(**12/14**= 50/1)

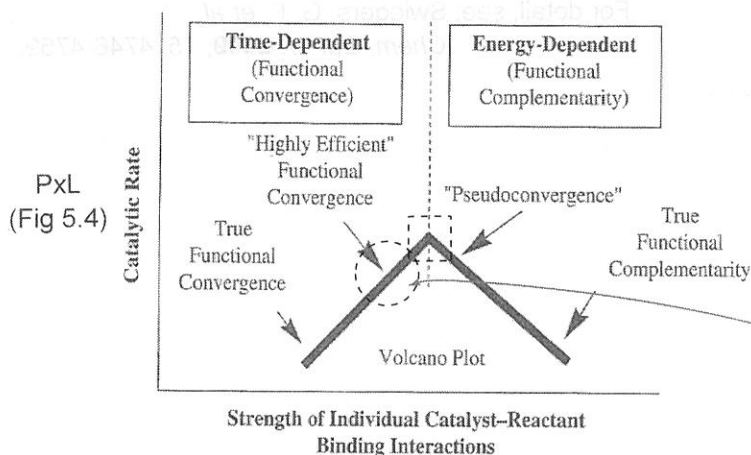- **13** catalysed the epoxidation with low selectivity. (**12/14**= 4/1)

  → *No absolute requirement* of cyclodextrin at this position.

- energy-dependent character
cyclodextrin groups offer an *additional* stabilization.

⟹ **pseudoconvergency**

✱ The spectrum of synergistic action in homogenous catalyst

   A continuum of action exists between functional convergence and complemetarity.

PxL
(Fig 5.4)

Figure 8.11. Hypothetical volcano plot for multicentered homogeneous catalysis.

- the 'best' catalyst will lie at the peak of the volcano plot.

   = the *dynamism of catalyst-reactant interactions* are perfectly balanced with *the thermodynamic efficiency*.

- selectivity would be better than comparable pseudoconvergent catalyst.
(← the weakness of its binding interactions would leave the reactants with insufficient time to participate in undesirable side reactions.)

◆ The goal is to achieve a balance between catalyst-reactant binding dynamism and thermodynamic efficiency.

✱ Designing of time-dependent homogeneous catalysts would be attractive.

<two qualification for design>

1) <u>Catalytic groups</u> must be suitable weakly and dynamically binding and activating.

2) <u>Their structual arrangement with respect to each other</u> should be driven by conformational flexing about a structure that is complementary to the TS of the reaction.

designing spatiotemporally

space + time
(dynamics)

✱ Where to start?
How to achieve the development of time-dependent catalyst has not established yet.

- from a natural time-dependent catalyst

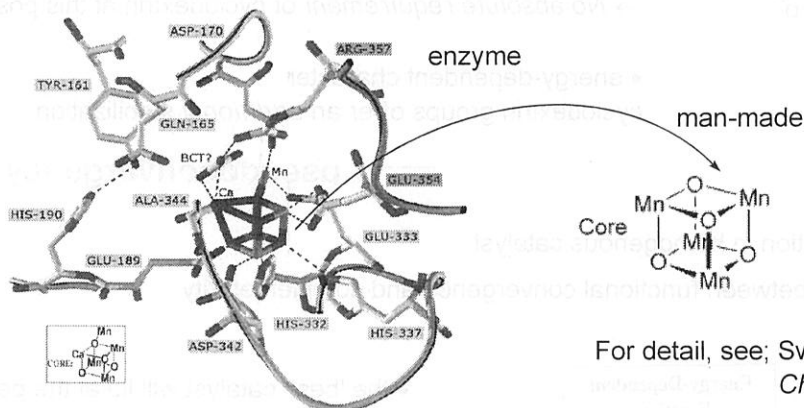catalytic groups which enzyme utilizes may be a good candidate.

ej.

enzyme

man-made

Core

Figure 5. XRD model of photosystem II water-oxidizing complex (PSII-WOC) showing a proposed model of the core active site.

(a)
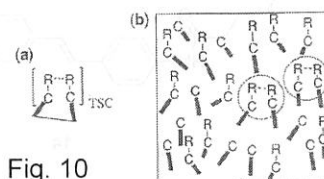
(b)

Fig. 10

<Statistical proximity effects>
→ *high concentration*
condition might be better.

For detail, see; Swiegers, G. F. *et al.*
Chem. Eur. J. **2009**, *15*, 4746-4759.