Fundamentals:

Basics for Designing Organic Nanomaterials

Chapter 1. Characteristics of Nanomaterials

Chapter 2. Methodology of Nanomaterials

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2.1.1. Microemulsion
2.1.2. Nanostructured Polymer (Copolymer, Dendrimer, DNA)
2.1.3. Nanostructured Ceramics (AAO, Porous Silica, Zeolite)

2.2. Non-template Method
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Chapter 3. Structure, Property, and Applications of Organic Nanomaterials
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3.2. 1-D Organic Materials
3.3. 2-D Organic Materials
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   - 5.3. DNA-templated synthesis

1. Microstructure based on block copolymers

1.1 Definition of copolymers

: polymer having more than two different repeat units.

~ABABABABABAABABABABA~

(Alternating copolymer)

~AABABBABAAABBABBBAAB~

(Random copolymer)

~AAAAAAAAAAAAAAAAAAAAA~
B
B
B
B
B
B
B
~

(Graft copolymer)

~AAAAAAAAAABBBBBBBBBB~

(Block copolymer)

A_mB_p diblock

$A_mB_pA_m$ triblock

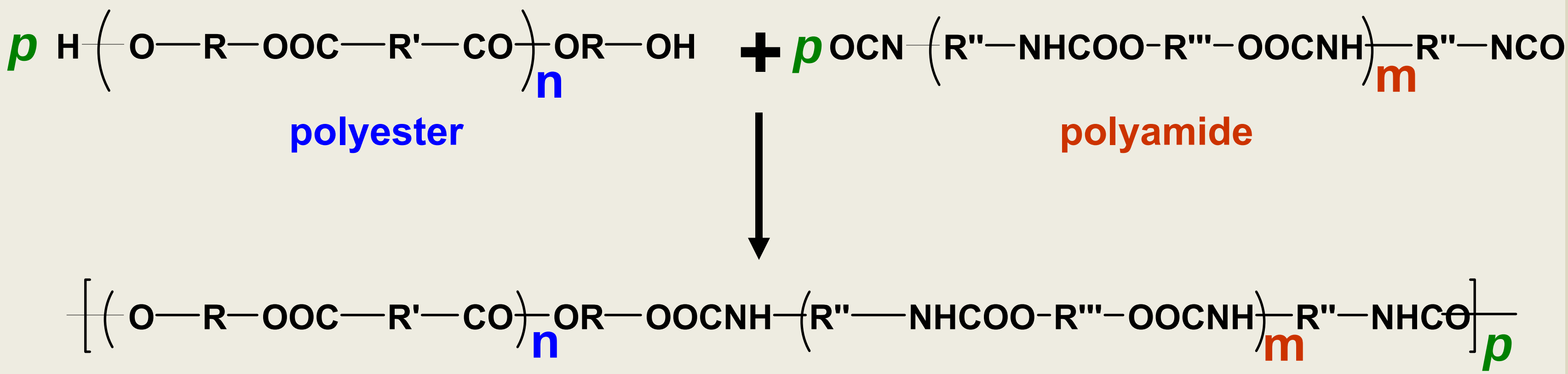
$A_mB_pA_mB_p$ tetrablock

$(A_mB_p)_n$ multiblock

A, B: repeating units

1.2 Synthesis Methods for Block Copolymers

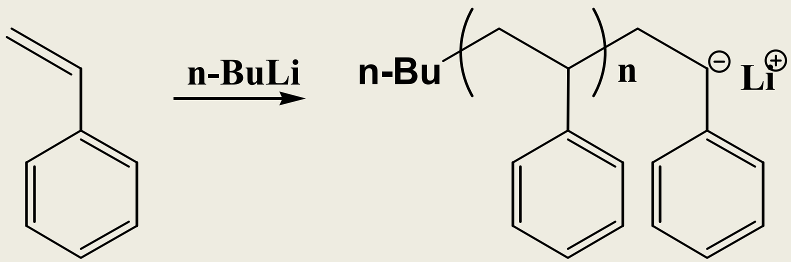
- **Step copolymerization**
  → The reaction between two different functional end groups of polymers



1. Microstructure based on block copolymers

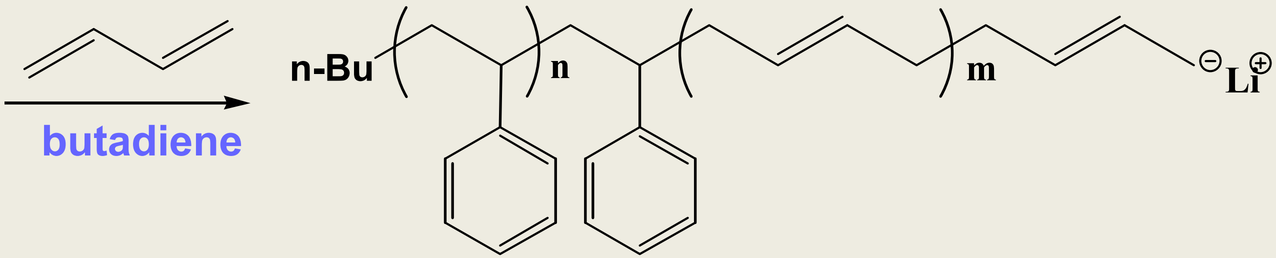
CNDL

- **Sequential polymerization (Anionic polymerization)**
  → A polymer is synthesized by anionic polymerization. Another monomer is then added to the living polymer carbanions.



styrene

Polystyrene



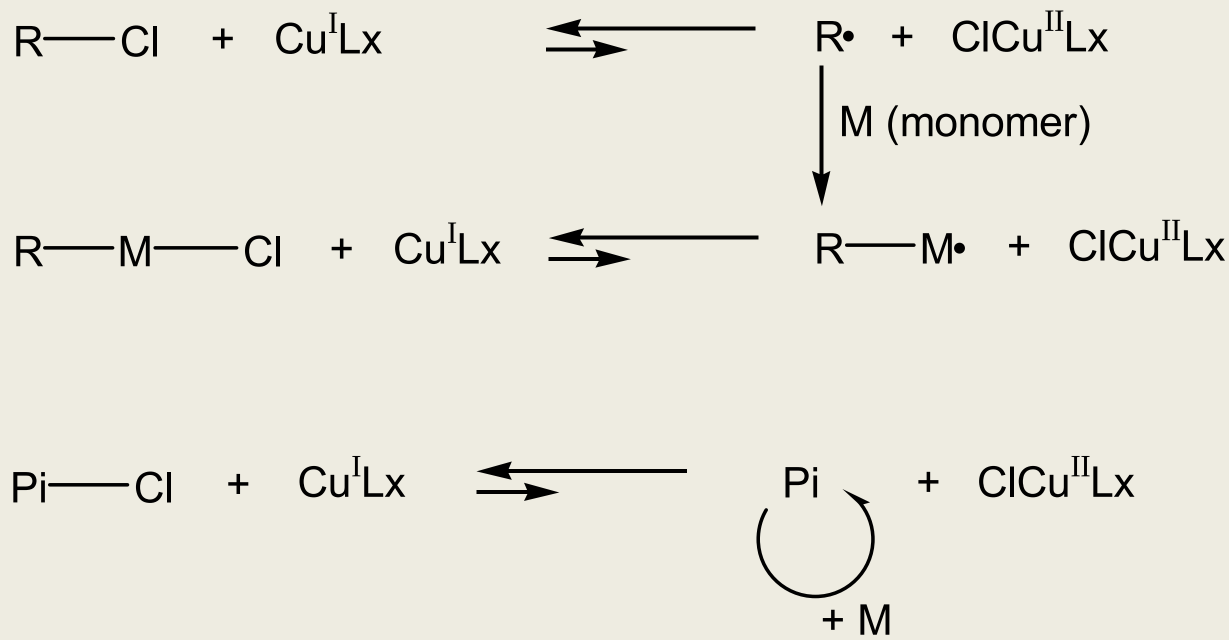
butadiene

Polystyrene-block-Poly(1,4-butadiene)

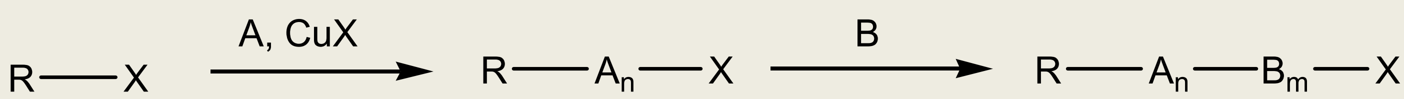
1. Microstructure based on block copolymers

❖ Sequential polymerization (Living radical polymerization)

▪ ATRP (Atom transfer radical polymerization)



▪ Copolymerization via ATRP



A, B ; monomer

1.3. Block Copolymer Aggregate and Self-assembly

❖ **Low-molecular-weight surfactants**

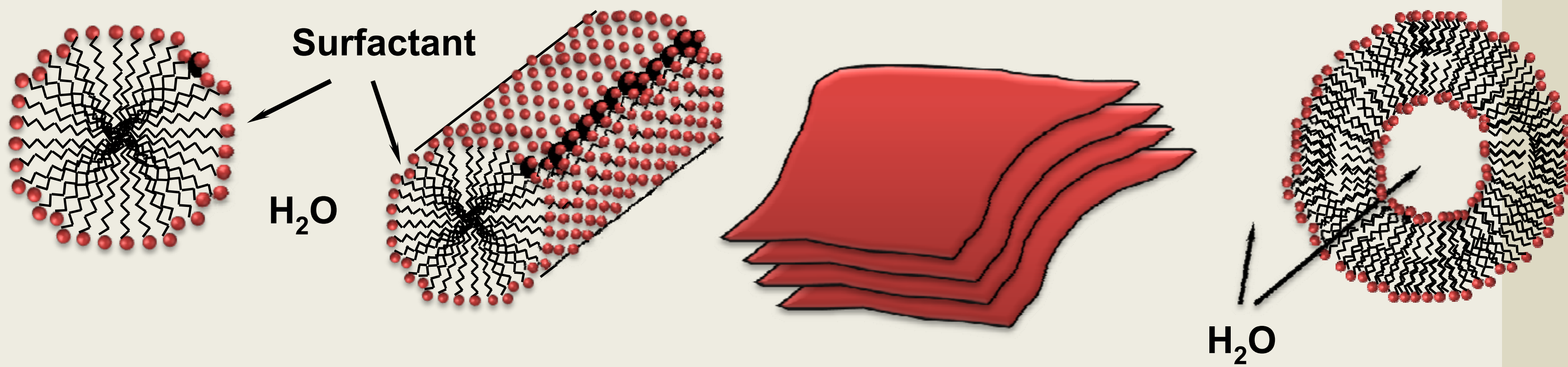
Hydrophobic tail
CH_3-CH_2-CH_2- …
CF_3-CF_2-CF_2- …

Hydrophilic head
$SO_3^-Na^+$
$NH_3^+Cl^-$
-$(OCH_2CH_2)_n$-

When surfactants are dissolved in water

- *reduce the surface tension because they are adsorbed on the surfaces*
- *form variety of aggregates – micelles, lamellae, vesicles, etc*

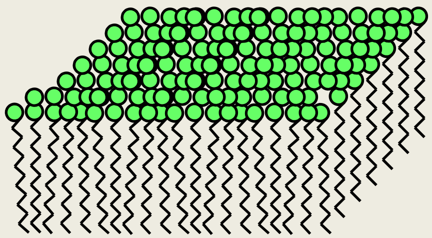
Spherical micelles **Cylindrical micelles** **Lamellae** **Vesicles**



1. Microstructure based on block copolymers

※Properties of the surfactant film

Surfactant film

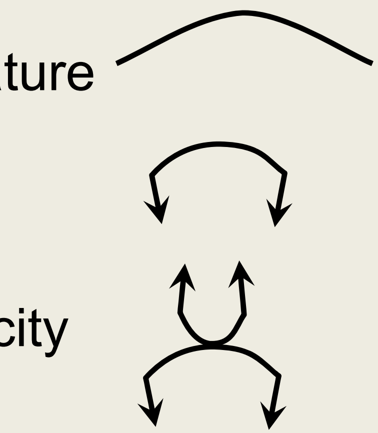


Properties of the surfactant film change with:

- Molecular structure
- Additives
- Ionic strength
- Co-surfactant
- Temperature, pressure etc.

Properties of the surfactant film:

- Interfacial tension
- Lateral elasticity
- Spontaneous curvature
- Bending elasticity
- Saddle splay elasticity



1. Microstructure based on block copolymers

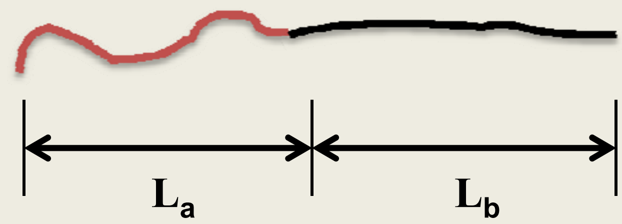
CNDL

❖ **Block copolymer & Low-molecular-weight surfactant**

Surfactant

≒

Block copolymer



More than two polymeric units (different solubility)

HLB value (hydorphilic-liphophilic balance)
Geometrical factor (size)
→ **ref. microemulsion chapter**

Length and ratio of polymer segments

Like surfactant, block copolymers can form various aggregates as varied polymer segments.

※ HLB Concept (Microemulsion chapter)

CNDL

- In an attempt to extend it into some kind of quantitative relationship between surfactant hydrophilicity and function in solution, Griffin introduced the concept of the hydrophilic-lipophilic balance (HLB) of a surfactant.
- Griffin's HLB numbers were restricted to non-ionic surfactants.

An arbitrary scale of 0 to 20 :
: 0 ~ completely hydrophobic molecule
20 ~ completely hydrophilic molecule

Table. Use of Griffin's HLB number concept

HLB number range	Appearance of aqueous solution
1–4	No dispersibility
3–6	Poor dispersibility
6–8	Milky dispersion after agitation
8–10	Stable milky dispersion
10–13	From translucent to clear
13–20	Clear solution

HLB number range	Application
3–6	w/o Emulsifier
7–9	Wetting agent
8–14	o/w Emulsifier
9–13	Detergent
10–13	Solubilizer
12–17	Dispersant

Ref.) W.C.Griffin, Journal of the Society of Cosmetic Chemists, 1949, 1, 311
W.C.Griffin, Journal of the Society of Cosmetic Chemists, 1954, 5, 259

※ HLB Concept (Microemulsion chapter)

- Griffin's HLB number concept was later extended by Davies, who introduced a scheme to assign HLB numbers to chemical groups which compose as surfactant.

Determination of HLB numbers according to Davies

Group	HLB number
Hydrophilic	
$-SO_4Na$	35.7
$-CO_2K$	21.1
$-CO_2Na$	19.1
$-N$ (tertiary amine)	9.4
Ester (sorbitan ring)	6.3
Ester (free)	2.4
$-CO_2H$	2.1
$-OH$ (free)	1.9
$-O-$	1.3
$-OH$ (sorbitan ring)	0.5
Lipophilic	
$-CF_3$	−0.870
$-CF_2-$	−0.870
$-CH_3$	−0.475
$-CH_2-$	−0.475
$-CH-$	−0.475
$-CH-$	

HLB =
7 + ∑ (hydrophilic group numbers)
+ ∑ (lipophilic group numbers)

Ref.) K.Holmberg, Surfactants and polymers in aqueous solution, 2nd Ed., John Wiley & Sons Ltd, England, 2003, p.460

J.T.Davies, Proceedings of the International Congress of Surface Activity, 1957, 426-438

"The HLB method of selecting an emulsifier is crude but simple."

- Some general guidelines for the selection of surfactants as emulsifier

(1) The surfactant should have a strong tendency to migrate to the oil-water interface.
(2) Oil-soluble surfactants preferably form w/o emulsions, and vice versa.
(3) Good emulsions are often formed by using a mixture of one hydrophilic and one hydrophobic surfactant.
(4) The more polar the oil phase, then the more hydrophilic the emulsifier should be, and vice versa.

Table. The use of the HLB method in selecting an emulsifier.

Emulsification of a mixture of 20% paraffin oil (HLB=10) and 80% aromatic mineral oil (HLB=13) in water

HLB number of oil: $10 \times 0.20 + 13 \times 0.80 = 12.4$

A mixture of $C_{12}E_{24}$ with HLB = 17.0 and $C_{16}E_2$ with HLB = 5.3 is used. A 60:40 mixture of the two gives a surfactant HLB number as follows:

$17.0 \times 0.60 + 5.3 \times 0.40 = 12.3$

This surfactant combination is found to give excellent emulsion stability.

Ref. M.J.Rosen, Surfactants and interfacial phenomena, 2nd Ed., Wiley, New York, 1989, p.327

- The structures of micelle can be simply determined by the geometric factors of the surfactant at the interface.

- **Critical packing parameter (CPP)**

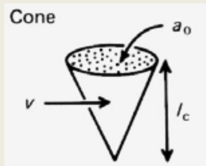
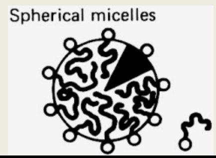
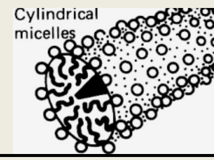
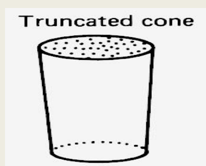
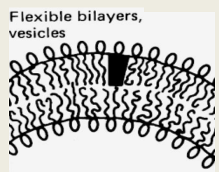
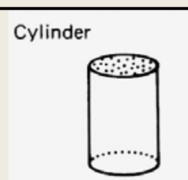
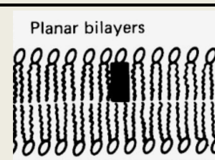
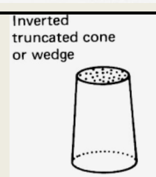
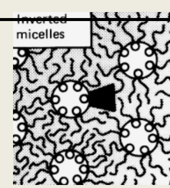
$$\frac{v}{a_0 l_c}$$

v : partial molecular volume of surfactant
a_o : area of head group of surfactant
l_c : maximum chain length

(1) Spherical micelles : CPP < 1/3
(2) Non-spherical micelles : 1/3 < CPP < 1/2
(3) Vesicles or bilayers : 1/2 < CPP < 1
(4) Inverted micelles : 1< CPP

- The change of environment (pH, temperature, ionic strength) will affect these parameters.

※ Geometric factor (Microemulsion chapter)

Packing parameter	Critical packing shape	Structures formed
<1/3		
1/3-1/2		
1/2-1		
~1		
>1		

-The relationship between aggregate type and geometry on the packing requirements of surfactant head group and chains

Ref. Intermolecular and Surface Forces, Israelachvili, Jacob N.

※ Geometric factor (Microemulsion chapter)

(1) Spherical micelles

- Usually formed by anionic surfactants
- For an o/w micelles, this can be done by adjusting the repulsion between head groups, resulting in large values for a_0.

(2) Cylindrical micelles

- It is a quite common phenomenon that micelles grow as the preferred surface curvature decreases. Any change that reduces the effective head group area will lead to the growth of micelles.
- Basic three ways to form cylindrical micelles

① addition of a cosurfactant with a very compact head group (i.e. n-alkanol)

② changing the counterion (i.e. changing Na^+ to Mg^{2+} reduce the effective volume of head groups.)

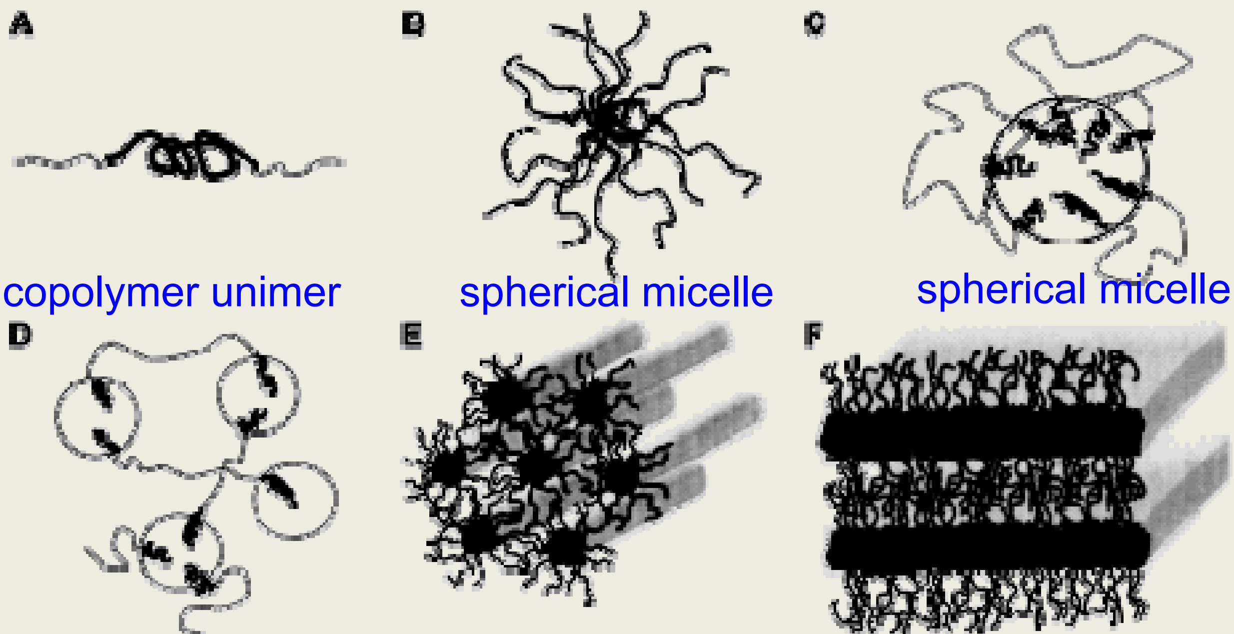
③ by electrolyte addition or temperature change (i.e. reduce the area of the head groups)

1. Microstructure based on block copolymers

❖ **Micelle formation of block copolymer**

; A solvent that is good for one of the units but poor for the other(s) leads to an amphiphilic behavior. (similar to low-molecular-weight surfactant solution)

; Block copolymer micelles are aggregates that resemble many properties of micelles formed by low-molecular weight surfactants.



copolymer unimer — spherical micelle — spherical micelle

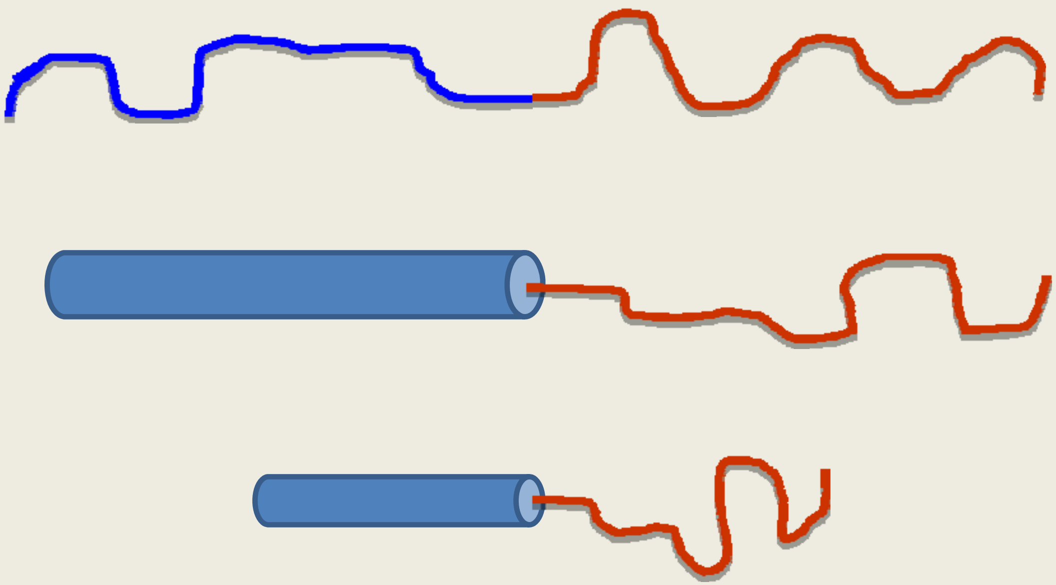
spherical micelle — cylindrical micelle — lamellar structure

1. Microstructure based on block copolymers

❖ **Self-assembly of Block copolymer based on type of polymer segments**

; The types of polymer segments can affect block copolymer aggregation. (self-assembly)

; Three different classes of diblock copolymer type will be discussed in this section.



Coil-coil diblock copolymer

Rod-coil diblock copolymer
(Total MW > 20,000 g/mol)

Rod-coil diblock oligomer
(Total MW < 20,000 g/mol)

1. Microstructure based on block copolymers

- **Coil-coil diblock copolymers**

; Block copolymers comprised of two flexible, chemcally incompatible and dissimilar blocks can microphase separated into a variety of morphologies.
eg) Polystyrene-*b*-Polyisoprene

; The degree of microphase separation is determined by χN.
→ χ : Flory interaction parameter,
a measure for the incompatibility between the two block,
be written in terms of solubility parameter(δ)

$$\chi = \frac{V_0}{kT}(\delta_A - \delta_B)^2 \quad \delta_A = \sqrt{\frac{\Delta E_A}{V_A}}$$

V_o : the lattice site volume
k : Boltzmann constant
T : temperature
ΔE_A : the evergy of vapourization of A molecule
V_A : molecular volume of A units

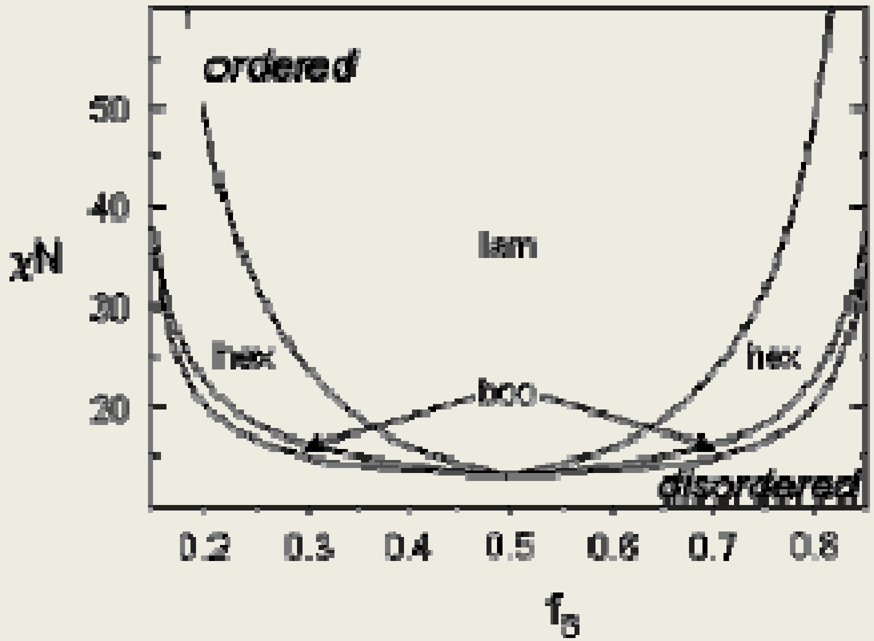
※ Solubility parameter ↔ cohesive energy density, interaction energy per unit volume between the molecules

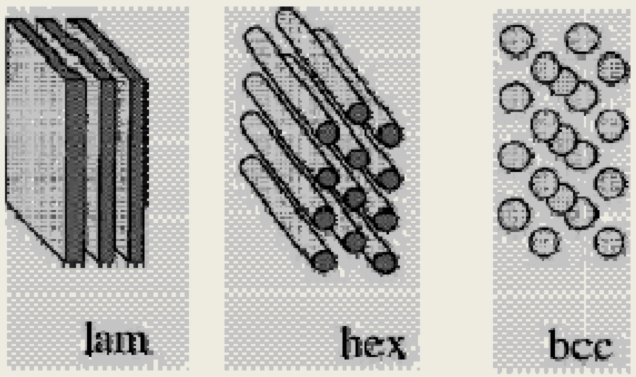
→ N : Total degree of polymerization, $N=N_A+N_B$

1. Microstructure based on block copolymers

; Separated morphology can be varied from spheres via lamellae to inverse spheres by changing the volume fractions of the blocks (*f*).

※ Experimental phase diagram for polystyrene-b-polyisoprene





→ f_s : **volum fraction of styrene segment**

$\chi N \leq 10$, weak-segregation limit

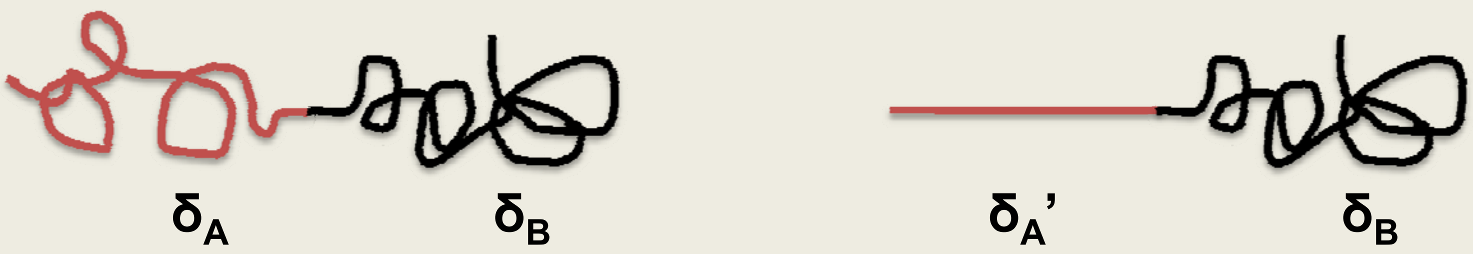
$10 < \chi N \leq 50$, intermediate segregation region

$\chi N \rightarrow \infty$, strong segregation limit

- **Rod-coil diblock copolymers**

; Replacing one of the blocks of a coil-coil diblock copolymer by a stiff, rigid segment results in a rod-coil type diblock copolymer.
eg) poly(*p*-phenylene)-*b*-poly(styrene), poly(phenylquinoline)-*b*-poly(styrene), poly(heyl isocyanate)-*b*-poly(styrene)

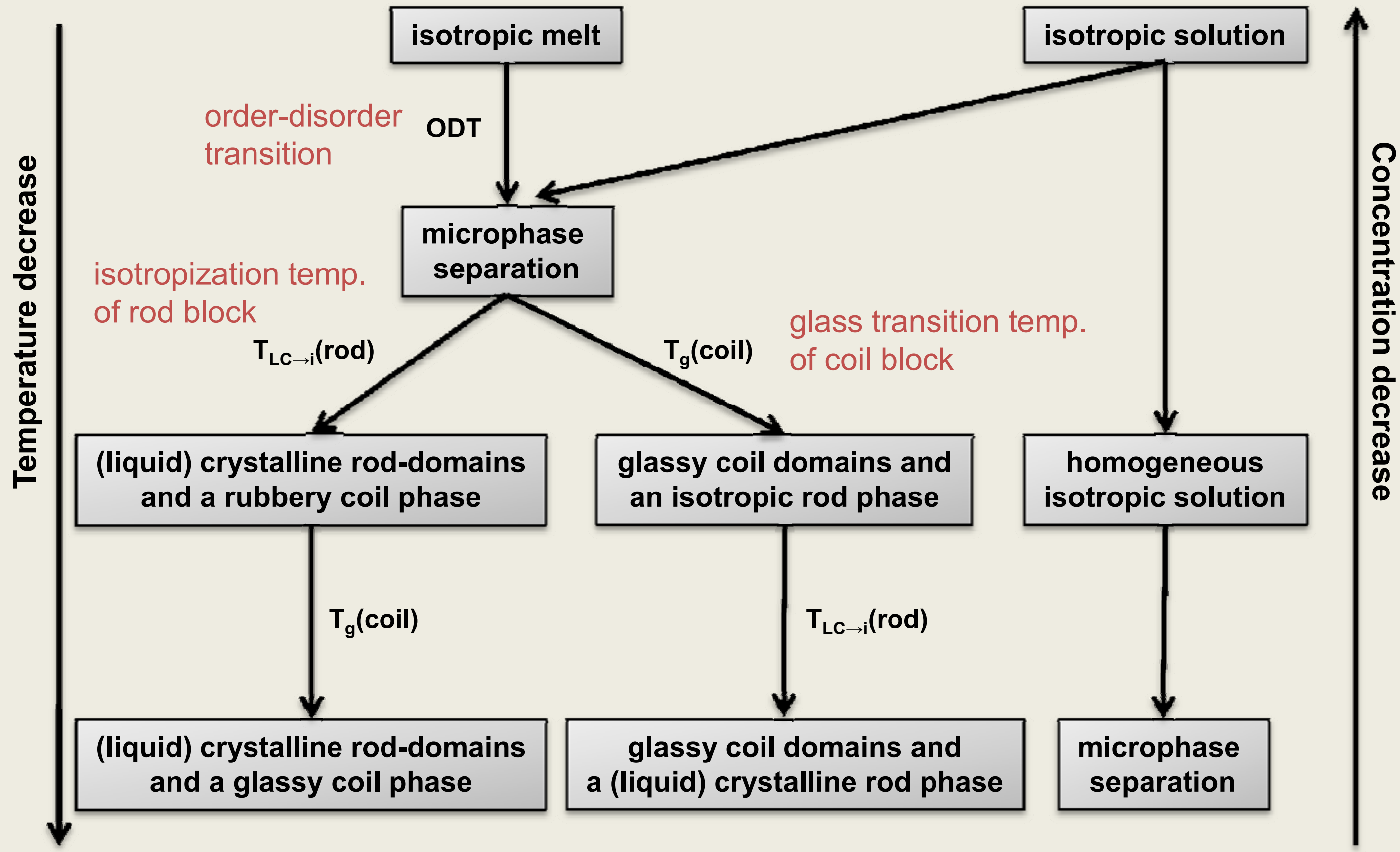
; The self-assembly is no longer solely determined by phase-separation, but is also affect by several other process.
→ aggregation of the rigid segments into (liquid-)crystalline domains
→ increase in the Flory interaction parameter due to stiffness asymmetry



$(\delta_A' - \delta_B)^2 > (\delta_A - \delta_B)^2$ ∴ χ is increased in rod-coil diblock copolymers

1. Microstructure based on block copolymers

※ **Possible routes for the self-assembly of rod-coil type diblock copolymer**



Ref. Klok et al. *Advanced materials*, **13** (2001) 1217

1. Microstructure based on block copolymers

; Cooling from an isotropic melt

1) The system passes ODT and undergo microphase separation

2) If $T_{LC \rightarrow i}$ of rod > T_g of coil,
further cooling 1 - formation of (liquid-)crystalline domains
surrounded by a layer of rubbery coils
further cooling 2 - (liquid-)crystalline domains of rod segments
surrounded by glassy phase of coil segments

If $T_{LC \rightarrow i}$ of rod < T_g of coil,
further cooling 1 - formation of glassy matrix
further cooling 2 - crystallization of rod blocks can only take place in confined
domains imposed by the glassy matrix formed by the coils

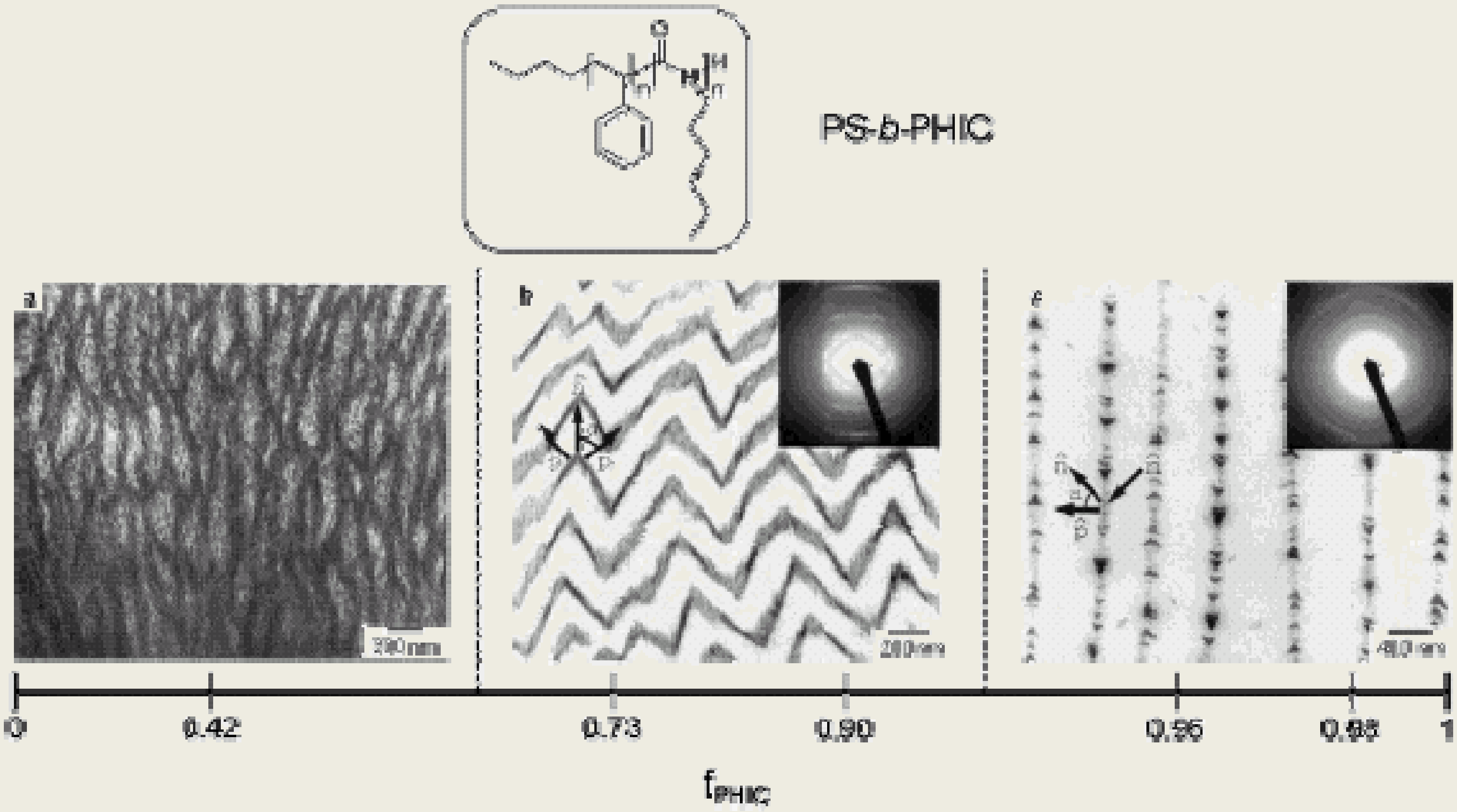
1. Microstructure based on block copolymers

; Evaporation of the solvent from isotropic solution

1) If a good solvent for both blocks is used,
microphase separation will continuously complete with crystallization of the rod segments during the evaporation of solvent until a stable structure is obtained.

2) If a good solvent for only one block is used,
the rod-coil block copolymers can already be pre-assembled into a particular supramolecular structure prior to film casting and evaporation of the solvent.

※ **Self-assembly of Poly(styrene)-*b*-poly(hexyl isocynate) with the volum fraction of hexyl isocynate segment (Rod portion)**



1. Microstructure based on block copolymers

CNDL

- **Rod-coil diblock oligomers**

; Like rod-coil diblock copolymer, the oligomers also indicates the competition between microphase separation of the blocks and aggregation of the rigid rods.

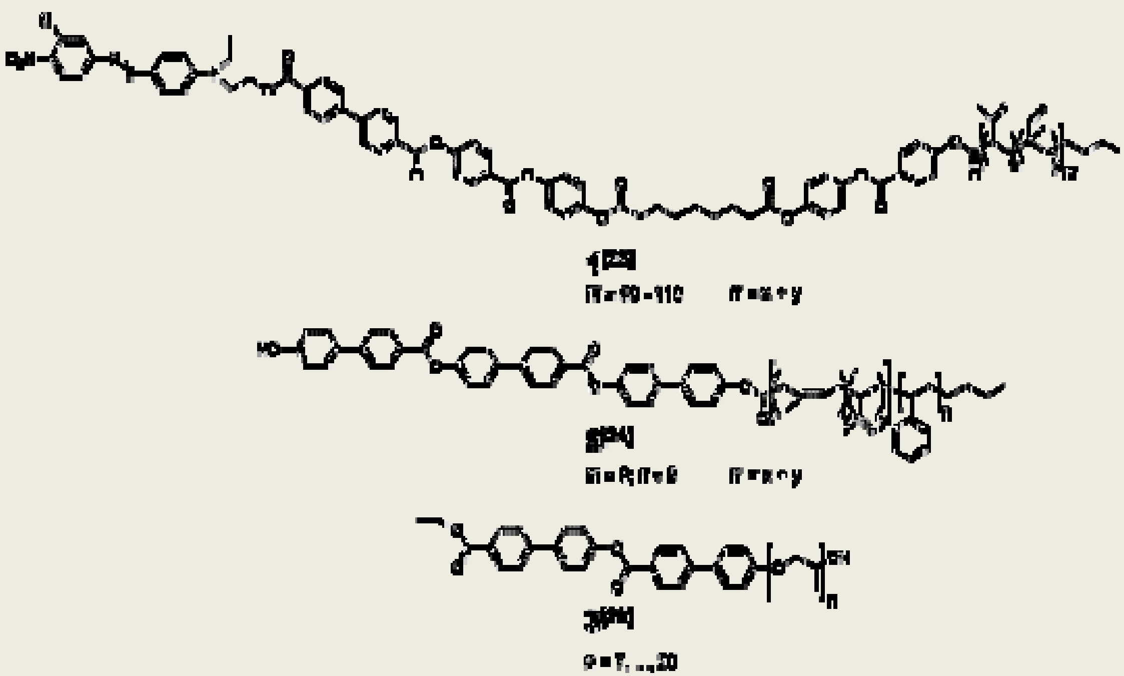
→ increase in the Flory interaction parameter due to their stiffness-asymmetry
→ Rod-coil diblock oligomers can allow access to phase-separated morphologies with domain sizes that can not be attained with traditional coil-coil diblock copolymers.

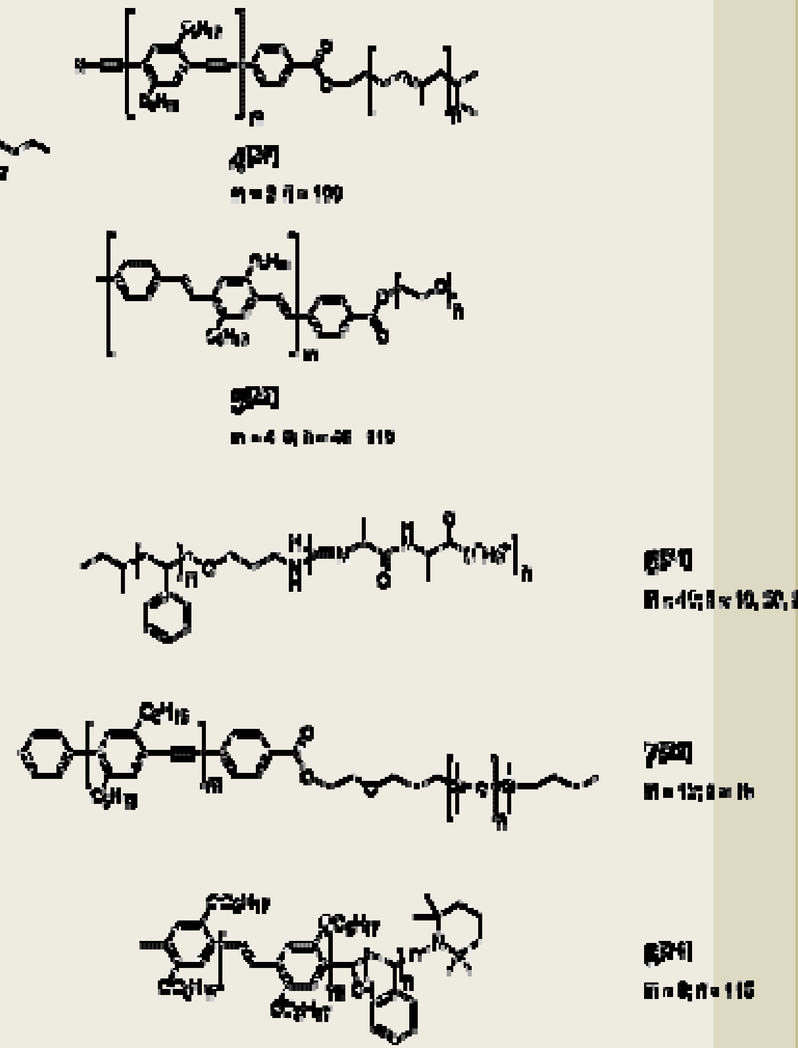
; Rod-coil diblock copolymers can be divided into two major classes.

→ i) perfectly monodisperse rod-segments, ii) polydisperse rigid rod
→ Diblock oligomers can be simply synthesized by organic reactions, so monodisperse rod-segments can be obtained.
cf) Polymer's MW is polydisperse

※ Polydispersity (MW) is known to have a strong influence on the liquid crystalline properties of rod-like macromolecules.

1. Microstructure based on block copolymers





※ **Example of rod-coil oilgomers**

Ref. Klok et al. *Advanced materials*, **13** (2001) 1217

2.1 Copolymer Composition

- We begin our discussion of copolymers by considering the free-radical polymerization of a mixture of two monomers, M_1 and M_2.
  → Growth mechanisms can be responsible for copolymer formation

- The polymerization mechanism: four distinctly different propagation reactions

$$-M_1\cdot + M_1 \xrightarrow{k_{11}} -M_1M_1\cdot \qquad -M_2\cdot + M_1 \xrightarrow{k_{21}} -M_2M_1\cdot$$

$$-M_1\cdot + M_2 \xrightarrow{k_{12}} -M_1M_2\cdot \qquad -M_2\cdot + M_2 \xrightarrow{k_{22}} -M_2M_2\cdot$$

- The rate laws governing these four reactions

k_{11}: 1st subscript → repeat unit in growing radical; 2nd subscript → adding monomer

$$R_{p,11} = k_{11}[M_1\cdot][M_1] \qquad R_{p,21} = k_{21}[M_2\cdot][M_1]$$

$$R_{p,12} = k_{12}[M_1\cdot][M_2] \qquad R_{p,22} = k_{22}[M_2\cdot][M_2]$$

- The customary assumption
  : the kinetic constants are independent of the size of the radical
  : the concentration of all radicals are indicated whatever their chain length, ending with the M_1 repeat unit by the notation $[M_1\cdot]$
  → only the nature of the radical chin end influences the rate constant for propagation

- the rate of monomer M_1, M_2 conversion to polymer

$$-\frac{\mathrm{d}[M_1]}{\mathrm{dt}} = k_{11}[M_1\cdot][M_1] + k_{21}[M_2\cdot][M_1]$$

$$-\frac{\mathrm{d}[M_2]}{\mathrm{dt}} = k_{12}[M_1\cdot][M_2] + k_{22}[M_2\cdot][M_2]$$

- the relative rates of the two monomer additions and the ratio of the two kinds of repeat units in the copolymer

$$\frac{\mathrm{d}[M_1]}{\mathrm{d}[M_2]} = \frac{k_{11}[M_1\cdot][M_1] + k_{21}[M_2\cdot][M_1]}{k_{12}[M_1\cdot][M_2] + k_{22}[M_2\cdot][M_2]}$$

- The stationaty-state approximation (total concentration of radicals is constant) ; $R_{p,21} = R_{p,12}$

$$k_{12}[M_1\cdot][M_2] = k_{21}[M_2\cdot][M_1] \quad \text{or} \quad \frac{[M_1\cdot]}{[M_2\cdot]} = \frac{k_{21}[M_1]}{k_{12}[M_2]}$$

$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1]}{[M_2]}\frac{(k_{11}/k_{12})[M_1]+[M_2]}{(k_{22}/k_{21})[M_2]+[M_1]}$$

$$r_1 = \frac{k_{11}}{k_{12}} \quad r_2 = \frac{k_{22}}{k_{21}}$$

$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1]}{[M_2]}\frac{r_1[M_1]+[M_2]}{r_2[M_2]+[M_1]} = \frac{1+r_1[M_1]/[M_2]}{1+r_2[M_2]/[M_1]}$$

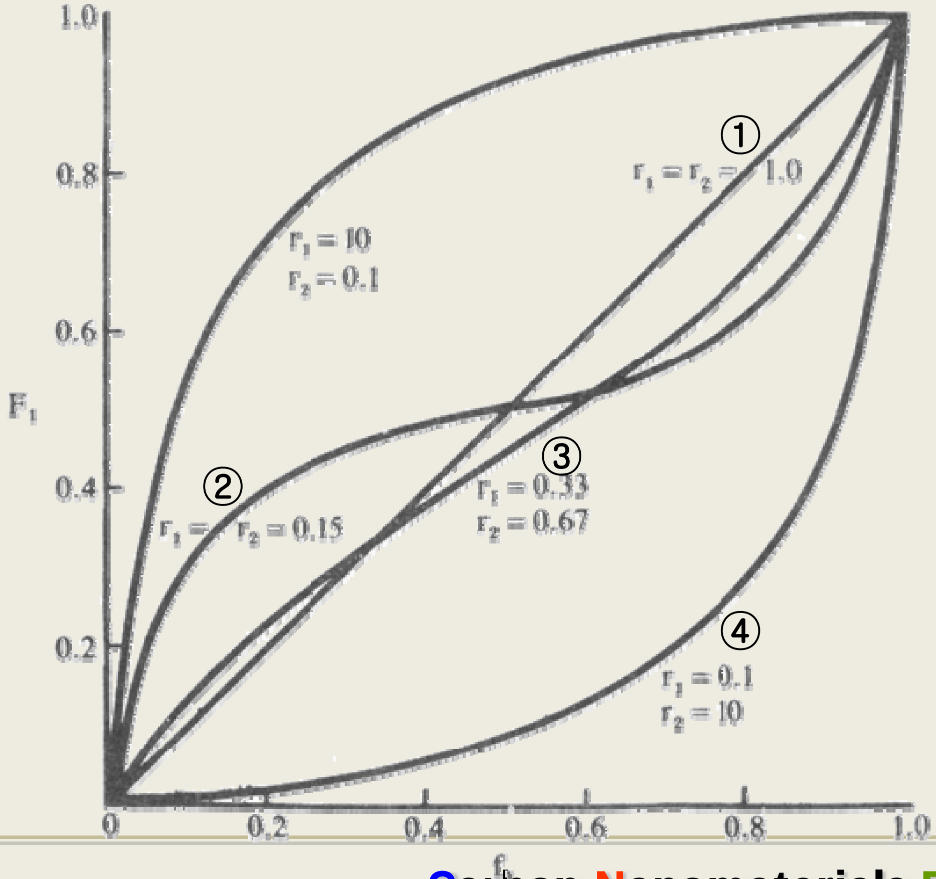
- Defining F_i as the mole fraction of the ith component in the polymer and f_i as the mole fraction of component i in the monomer solutions

$$F_1 = 1 - F_2 = \frac{d[M_1]}{d[M_1]+d[M_2]}$$

$$f_1 = 1 - f_2 = \frac{[M_1]}{[M_1]+[M_2]}$$

$$F_1 = \frac{r_1 f_1^2 + f_1 f_2}{r_1 f_1^2 + 2 f_1 f_2 + r_2 f_2^2}$$

→ This equation relates the composition of the copolymer formed to the instantaneous composition of the feedstock and to the parameters r_1 and r_2 which characterize the specific system.



① $r_1=r_2=1$

: copolymer and the feed mixture have the same composition at all times : $F_1 = f_1$

② $r_1=r_2$

: copolymer and the feed mixture have the same composition at f=0.5 : $F_1 = 0.5$

③ $r_1 \neq r_2$

: The monomer ratio at crossover point

: For $r_1=0.33$, $r_2=0.67$ → $f_1=0.33$

④ $r_1=1/r_2$

2.2 Reactivity Ratios

- The parameters r_1 and r_2 are the vehicles by which the nature of the reactants enter the copolymer composition equation.
- Several important things to note about radical reactivity ratio.

① $r_1=k_{11}/k_{12}$; $r_1>1$ → M_1• adds M_1 in preference to M_2
; $r_1<1$ → M_1• adds M_2 in preference to M_1
② Although r_1 is descriptive of radical M_1•, it also depends on the identity of the other
→ To characterize a system the pair of parameters r_1 and r_2 are both required
→ the product r_1r_2 is used to quantify
③ The reciprocal of a radical reactivity ratio is used to quantitatively express the reactivity of monomer M_2 by comparing its rate of addition to radical M_1•
④ The radical reactivity ratio follows the Arrhenius equation with an apparent activation energy. (equal to the difference in the activation energies for the individual constants; $E_{app}^* = E_{p,\,11}^* - E_{p,\,12}^*$)

Table. Values of reactivity ratio r_1 and r_2 and the product r_1r_2 for a few copolymers at 60 ℃

M_1	M_2	r_1	r_2	r_1r_2
Acrylonitrile	Methyl vinyl ketone	0.61	1.78	1.09
	Methyl methacrylate	0.13	1.16	0.15
	A-Methyl styrene	0.04	0.20	0.008
	Vinyl acetate	4.05	0.061	0.25
Methyl methacrylate	Styrene	0.46	0.52	0.24
	Methacrylic acid	1.18	0.63	0.74
	Vinyl acetate	20	0.015	0.30
	Vinylidene chloride	2.53	0.24	0.61
Styrene	Vinyl acetate	55	0.01	0.55
	Vinyl chloride	17	0.02	0.34
	Vinylidene chloride	1.85	0.085	0.16
	2-Vinyl pyridine	0.55	1.14	0.63
Vinyl acetate	1-Butene	2.0	0.34	0.68
	Isobutylene	2.15	0.31	0.67
	Vinyl chloride	0.23	1.68	0.39
	Vinylidene chloride	0.05	6.7	0.34

2. General Theories of Block Copolymers

CNDL

- The products r_1r_2 lie in the range between 0~1.
- The product r_1r_2 → 0

① $r_1r_2 = 0$ and $r_1=r_2=0$; the copolymer adds monomers with perfect alternation.
→ No tendency for a radical to add a monomer of the same kind
② when only one of the r's is zero; alternation occurs whenever the radical ends with an M_1• unit → Tendency toward the alternation
∴ Increasing tendency toward alternation as r_1 →0 and r_2 →0, more succinctly, as the product r_1r_2 →0

- The product r_1r_2 → 1

: two monomers have the same relative tendency to add to both radicals
→ If r_1= 10, monomer 1 is 10 times as likely to add to M_1• than monomer 2
→ If r_2= 0.1, monomer 1 is 10 times as likely to add to M_2• than monomer 2
∴ The radicals exert the same influence; monomers add at random

- Recognition of these difference in behavior points out an important limitation on the copolymer composition equation.
→ *describes the overall composition of the copolymer, but gives no information about the distribution of the different kinds of repeat units within polymer*

CNDL

- It is possible that copolymers with the same overall composition have very different properties because of differences in microstructure.

  - *Alternating structure* by $r_1 \rightarrow 0$ and $r_2 \rightarrow 0$

$$M_1M_2M_1M_2M_1M_2M_1M_2M_1M_2M_1M_2M_1M_2M_1M_2M_1M_2$$

  - *Random structure* by $r_1r_2 \rightarrow 0$

$$M_1M_2M_2M_2M_1M_1M_2M_1M_1M_2M_1M_2M_1M_2M_1M_2M_2M_1$$

  - *Block structure* by $r_1r_2 > 1$

$$M_1M_1M_1M_1M_1M_1M_1M_1M_1M_2M_2M_2M_2M_2M_2M_2M_2M_2$$

- Each of these polymers has a 50:50 proportion, but differ in properties
  → As examples of such differences → Appendix 5-2

What factors in the molecular structure of two monomers govern the kinetics of the different addition steps?

2. General Theories of Block Copolymers

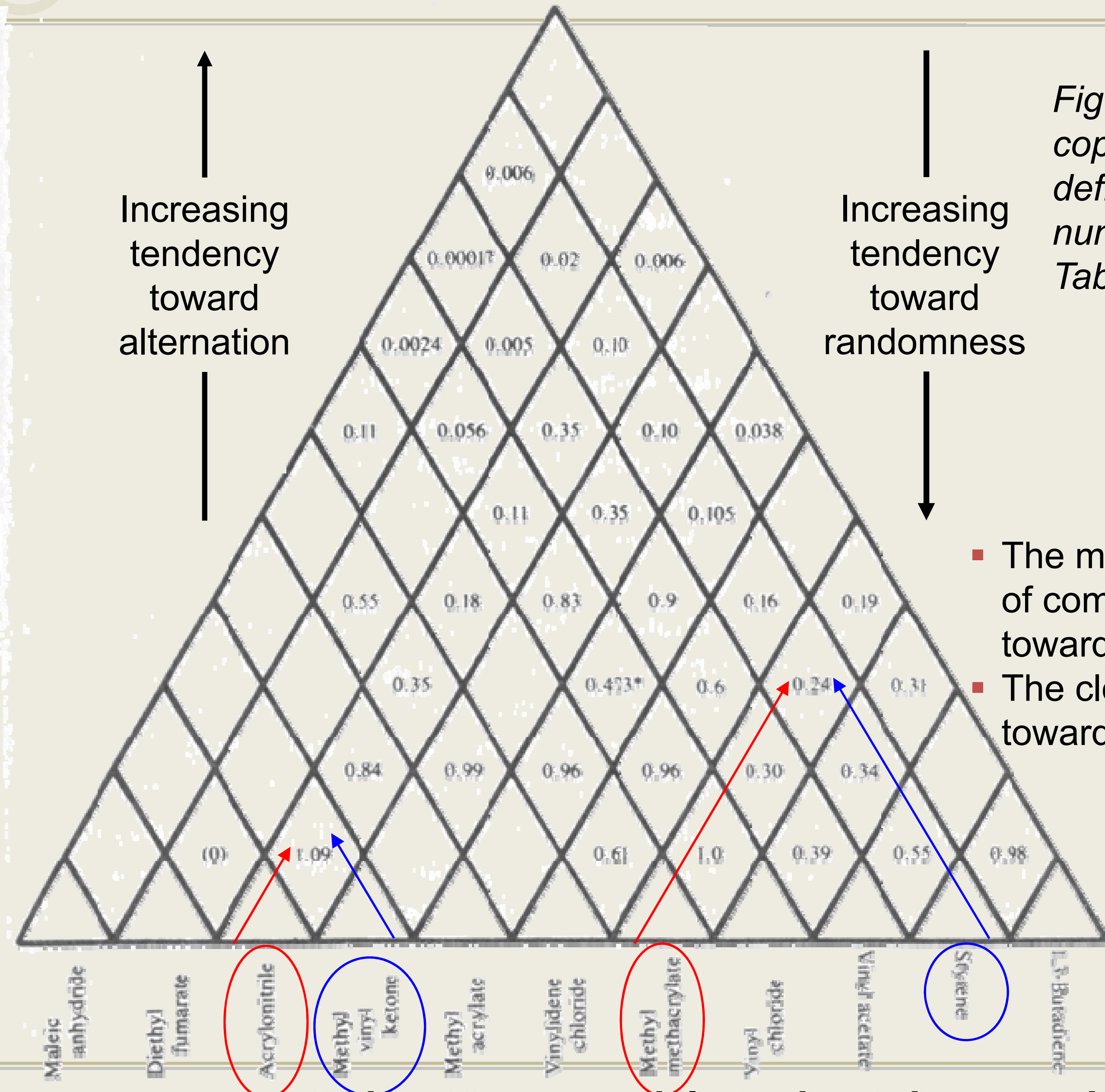
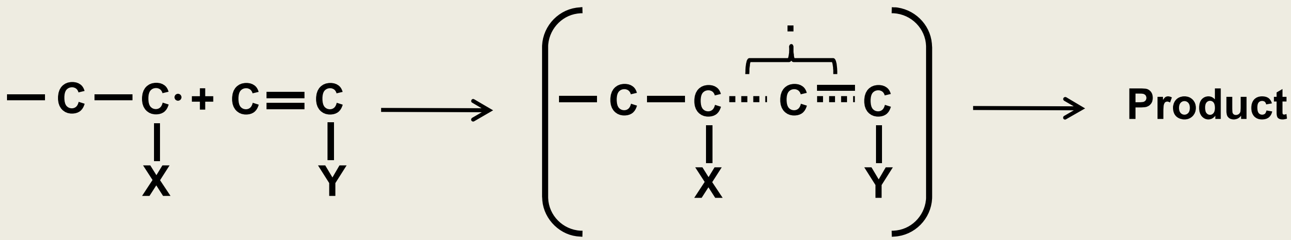


Fig . The product r_1r_2 for copolymers whose components define the interaction where the numbers appear. Data from Table and others

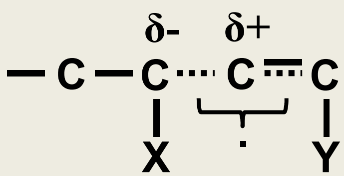
- The more widely separated a pair of comonomers → tendency toward alternation
- The closer together → tendency toward randomness

2.3 Resonance and Reactivity

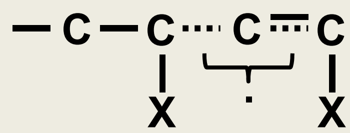


- The transition state for the addition of a vinyl monomer to a growing radical involves the formation of a partial bond between the two species.

(I)



(II)



- If X is an electron donor and Y an electron acceptor, then the partial bond in the transition state is stabilized by a resonance form (I) which attributes a certain polarity to the emerging bond. The contribution of this polar structure to the bonding lowers the energy of the transition state.
- The transition state for the successive addition of the same monomer (II) involves a more uniform distribution of charge because of the identical substituent and thus lacks the stabilizing effect of the polar resonance form. The activation energy for this mode of addition is greater than that for alternation, at least when X and Y are sufficiently different.

2. General Theories of Block Copolymers

- The activities of radicals and monomers → a source of insight into copolymer formation
- The reactivity of radical 1 copolymerizing with monomer 2 is measured by the rate constant k_{12}.

$$k_{12} = \frac{k_{11}}{r_1}$$

Table. Values of the cross-propagation constants k_{12} for four monomer-radical combinations

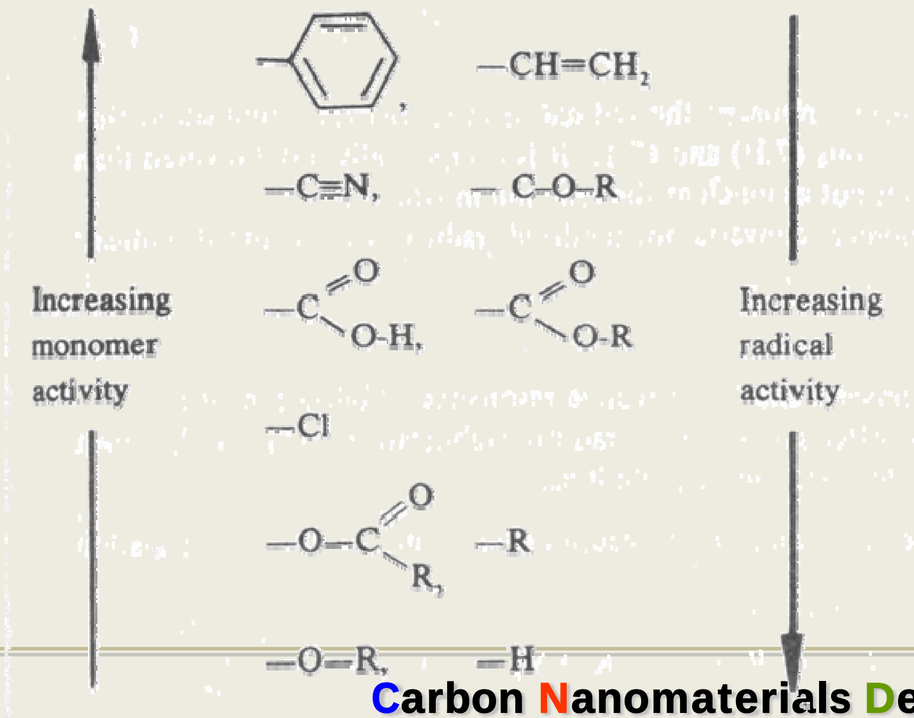
Monomer	Radical			
	Styrene	Acrylonitrile	Methyl acrylate	Vinyl acetate
Styrene	145	49,000	14,000	230,000
Acrylonitrile	435	1,960	2,510	46,000
Methyl acrylate	203	1,310	2,090	23,000
Vinyl acetate	2.9	230	230	2,300

2. General Theories of Block Copolymers

- Radical activity
  styrene < acrylonitrile < methyl acrylate < vinyl acetate

- Monomer reactivity
  styrene > acrylonitrile > methyl acrylate > vinyl acetate

Table. List of some substituents ranked in terms of their effects on monomer and radical reactivity



- Conjugated double bond
  → more stable as radicals and
  more reactive as monomers

- It is important to realize that the ability to form conjugated structures is associated with a substituent whether it is in a monomer or a radical

- Propagation constants (subscript rs: resonance stabilization)

$$R_{rs}\bullet + M < R_{rs}\bullet + M_{rs} < R\bullet + M < R\bullet + M_{rs}$$

Radical	Styrene		Styrene		Vinyl acetate		Vinyl acetate
	+	<	+	<	+	<	+
Monomer	Vinyl acetate		Styrene		Vinyl acetate		Styrene

- Resonance stabilization energies are generally assessed from thermodynamic data.
- Resonance stabilization energy of i species ➔ ε_i
- The heat of formation will be less by an amount ε_i than for an otherwise equivalent molecule without resonance.

$$\Delta H_{rs} = \Delta H_{no\ rs} - \Delta\varepsilon$$

2. General Theories of Block Copolymers

CNDL

- If we consider the homopolymerization of ethylene (no resonance possibilities)

$$-CH_2-CH_2\bullet + CH_2{=}CH_2 \rightarrow -CH_2CH_2CH_2CH_2\bullet$$

$$\Delta H_{no\ rs} = -88.7\text{kJ mol}^{-1}$$

- As a reference reaction, and compare it with the homopolymerization of styrene (resonance effect present)

$$-CH_2-\underset{\Phi}{\underset{|}{CH}}\bullet + CH_2{=}\underset{\Phi}{\underset{|}{CH}} \rightarrow -CH_2-\underset{\Phi}{\underset{|}{CH}}-CH_2\underset{\Phi}{\underset{|}{CH}}-$$

$$\Delta H_{rs} = -69.9\text{kJ mol}^{-1}$$

- A value of $\Delta\varepsilon$= -19 kJmol^{-1} → the negative value indicates the overall loss of resonance stabilization.
- The activation energy of reactions parallel their heats of reaction → E*= kΔH (k: an appropriate proportionality constant)

$$E_{11}^{*} - E_{12}^{*} = k\left[-\Delta\varepsilon_{11} - \left(-\Delta\varepsilon_{12}\right)\right]$$

$$= -\left(\varepsilon_{P_1\cdot} - \varepsilon_{R_1\cdot} - \varepsilon_{M_1}\right) + \left(\varepsilon_{P_2\cdot} - \varepsilon_{R_1\cdot} - \varepsilon_{M_2}\right)$$

2. General Theories of Block Copolymers

- The proportionality constant (k) →1, R_1• cancels out, and dependence of the reactivity ratio r_1 also involves the E_{11}^*-E_{12}^* difference through the Arrhenius equation;

$$r_1 \propto \exp\left(\frac{\varepsilon_{P_1\cdot} - \varepsilon_{M_1}}{RT}\right)\exp\left(\frac{-\left(\varepsilon_{P_2\cdot} - \varepsilon_{M_2}\right)}{RT}\right)$$

$$r_2 \propto \exp\left(\frac{\varepsilon_{P_2\cdot} - \varepsilon_{M_2}}{RT}\right)\exp\left(\frac{-\left(\varepsilon_{P_1\cdot} - \varepsilon_{M_1}\right)}{RT}\right)$$

- According to this formalism, the following applied:
  - 1. The reactivity ratios are proportional to the product of two exponential numbers
  - 2. Each exponential involves the difference between the resonance stabilization energy of the radical and monomer of a particular species
  - The positive exponent is associated with the same species as identifies the r (i.e., for r_1, M_1→P_1•), while the negative exponent is associated with the other species (for r_1, M_2→P_2•)

3.1 Block Copolymer Phase Behavior (in the "melt" state)

(1) One-component block copolymer system

- The different blocks of a block copolymer are able to segregate (microphase separation) and form domains with different morphologies.
- The stability of different morphologies
  → From an interplay between enthalpic (contact between chemically different blocks) and entropic (chain stretching, confinement, frustration) contribution to the system free energy.
  → Described in terms of a χN vs f phase (Fig)

χ : Flory-Huggins interaction parameter between the different blocks
→ Enthalpic contribution
N : degree of polymerization (copolymer molecular weight)
→ Tendency for block segregation → Entropic contribution
f : volume fraction of one block (composition variable)

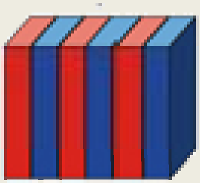
- The higher χN → higher degree of segregation between the different blocks
  → higher tendency for forming ordered microstructures
- Order-disorder transition : at $\chi N \approx 10.5$
- The morphologies (sphere, cylinder, lamellar) depend on the composition f

3. A Closer Look at Microstructure

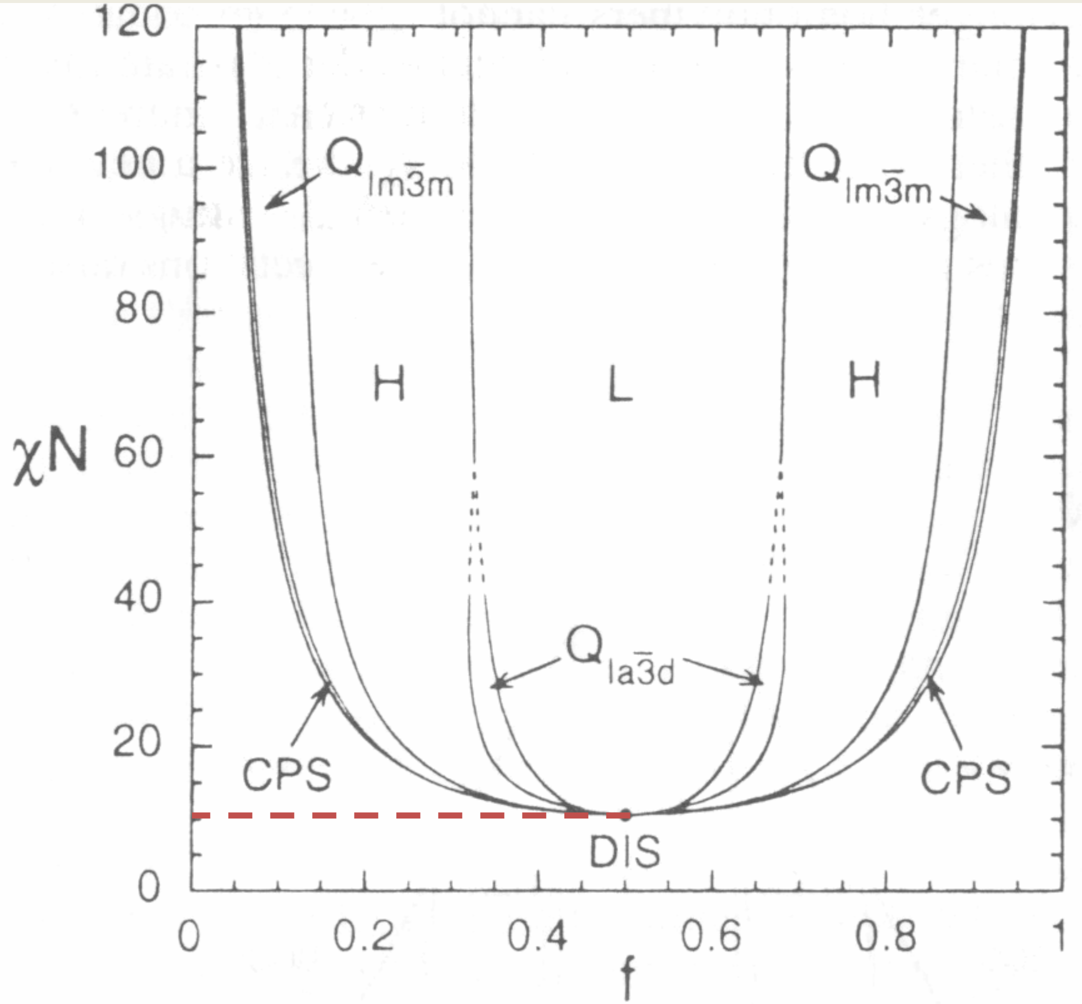
Fig. χN vs f phase diagram for symmetric AB block copolymer, predicted from mean-field theory. L (lamellar), H (hexagonal-packed cylinders), Q_{Ia3d} (gyroid), Q_{Im3m} (bcc spheres), CPS (close-packed FCC spheres), and DIS (disorderd).
Ref. M. W. Matsen and F. S. Bates, Macromolecules, 29 (1996) 478

Appendix 1

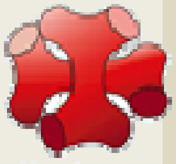
Lamellar



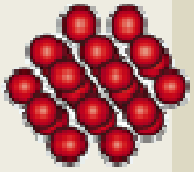
Hexagonal cylinder



Gyroid



Sphere



CNDL

(2) Two- and three-component block copolymer system

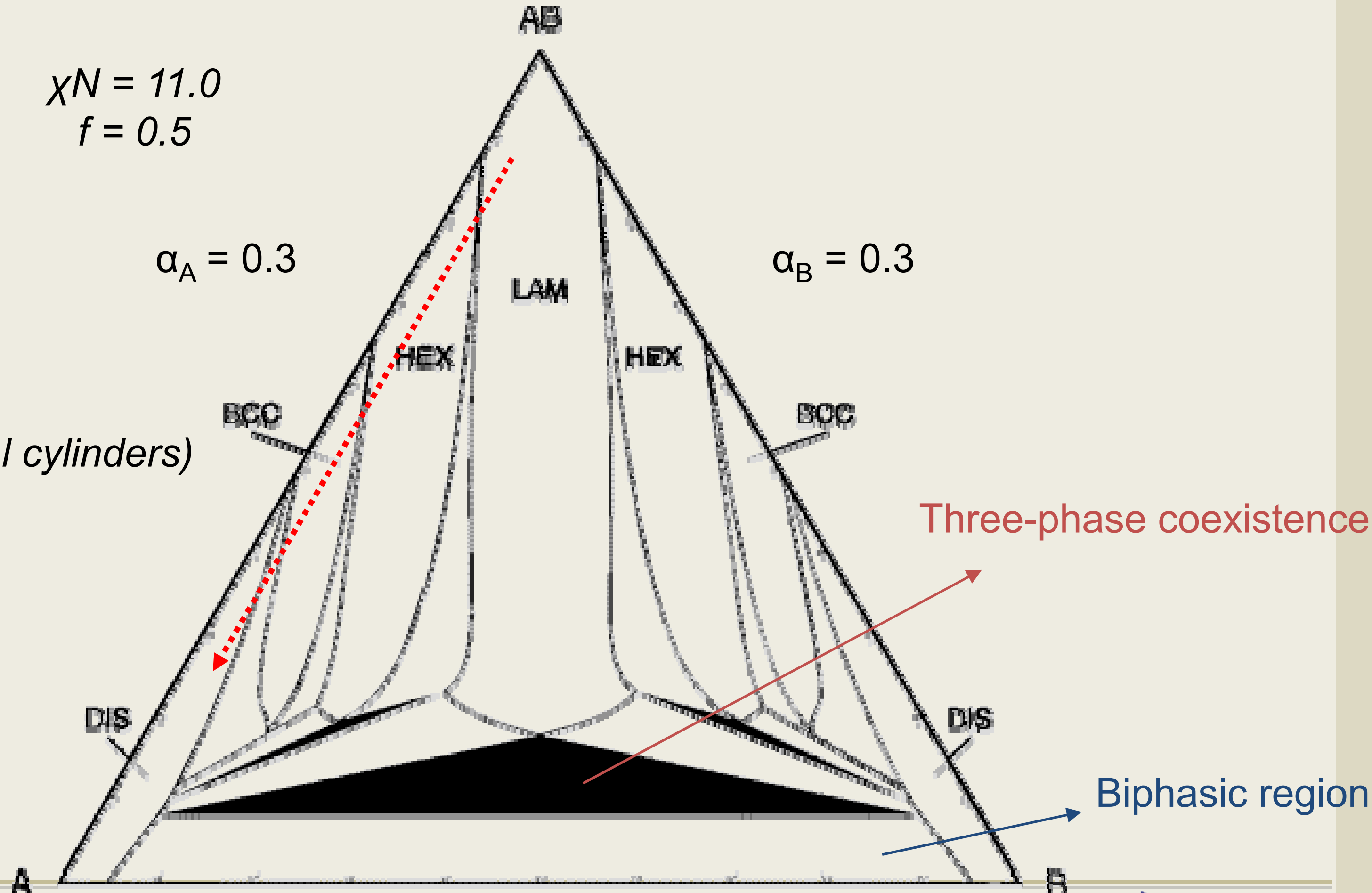
- The interfacial curvature in solvent-free block copolymers → by the composition *f*
  → At given block composition can result in only one type of microstructure
  → For different structures, different composition are required (synthesis of other polymers)
- Multicomponent system: homopolymer or copolymer added to a block copolymer
  → can result into a wide variety of morphologies
- For example, addition of an A-homopolymer to an AB-block copolymer
  → modifying the ratio of A and B: increase of A → shift the phase stability
  → predicting by self-consistent field theory (Appendix 2)

- Fig : isothermal (constant χN) phase diagram
  : AB-block copolymer + A-homopolymer + B-homopolymer
  → Morphologies change: lamellar → cylinder → sphere (red dotted line)

→ Reducing the need to synthesize a new block copolymer for a specific morphology

3. A Closer Look at Microstructure

Fig. Phase diagram for a symmetric AB-diblock copolymer (N) with an A-homopolymer (0.3N) and a B-homopolymer (0.3N), predicted from mean-field theory.
Three-phase coexistence; shaded and biphasic region; unlabeled
Ref. P. K. Janert and M. Schick, Macromolecules, 30 (1997) 137



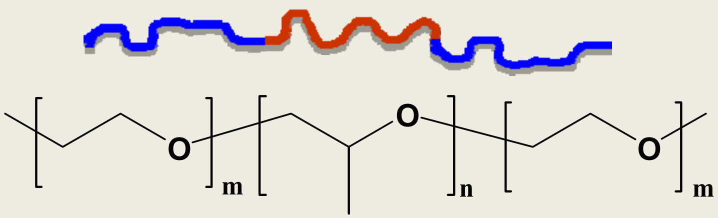
LAM (lamellar)
HEX (hexagonal cylinders)
DIS (disorderd).

3.2 Amphiphilic Block Copolymers in Mixtures with Water and Oil

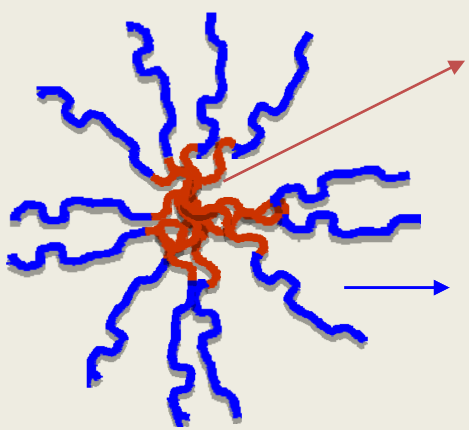
: The main features of the self-assembly of block copolymers in binary and ternary systems with solvents and effects on self-assembly of the block copolymer MW and composition

(1) Binary amphiphilic block copolymer - water system

PEO-PPO-PEO



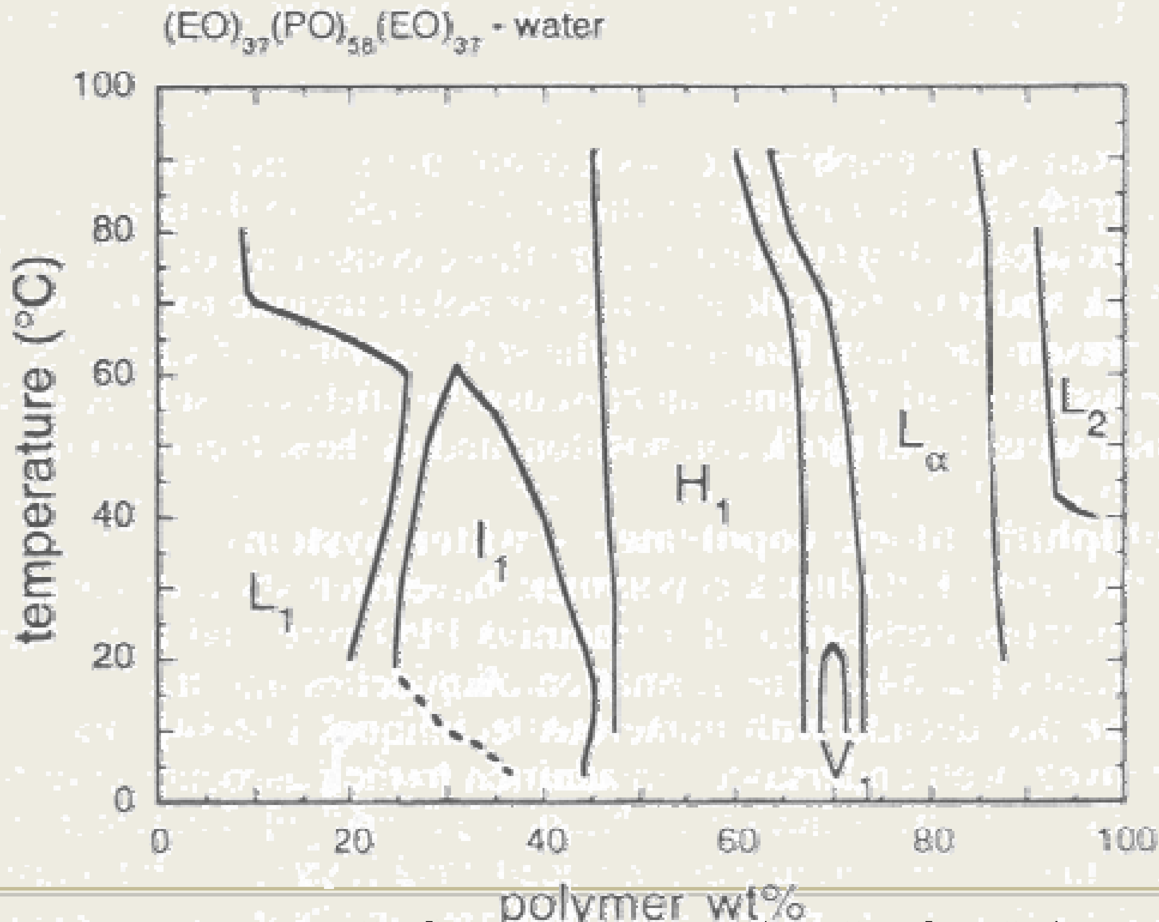
hydrophilic hydrophobic



- The temperature effects on the phase behavior of copolymers → understood by invoking the reverse solubility (temperature↑ → solubility↓)
- The temp.↑
  → PEO-water and PPO-water interaction parameter χ ↑
  → PEO-PPO interaction parameter χ↓
  → hydrophobicity of the polymer ↑
  → solubility ↓
- At Fig, Lα regions shift to lower polymer concentration as the temp ↑

3. A Closer Look at Microstructure

Fig. The concentration-temperature phase diagram of the $EO_{37}PO_{58}EO_{37}$ (Pluronic P105) block copolymer-H_2O binary system.
Ref. P. Alexandridis, D. Zhou, A. Khan, Langmuir, 12 (1996) 2690



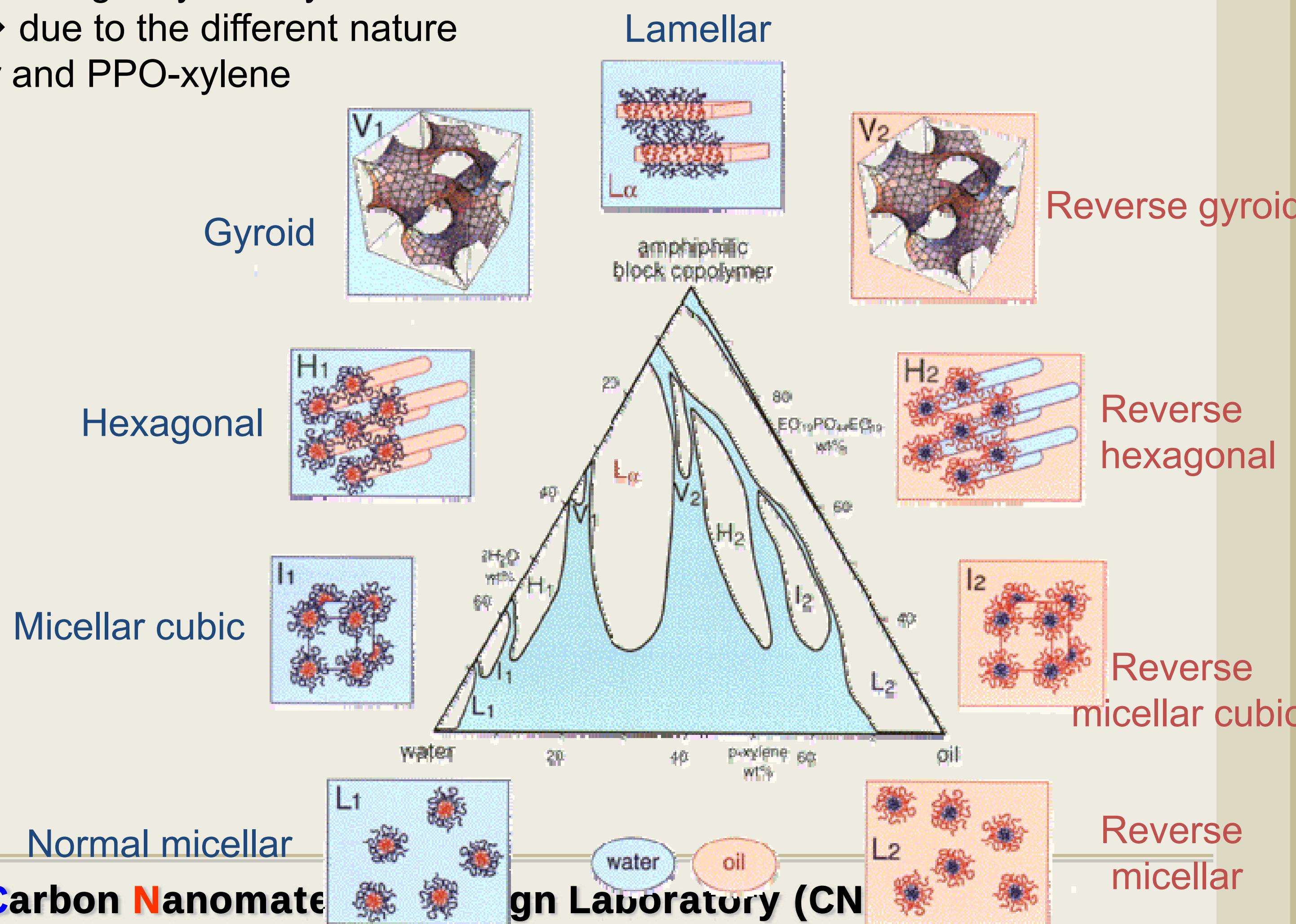
I_1 : micellar cubic
H_1 : hexagonal cylinder
V_1 : gyroid
L_α : lamellar
L_1 : water-rich solutions
L_2 : polymer-rich solutions

3. A Closer Look at Microstructure

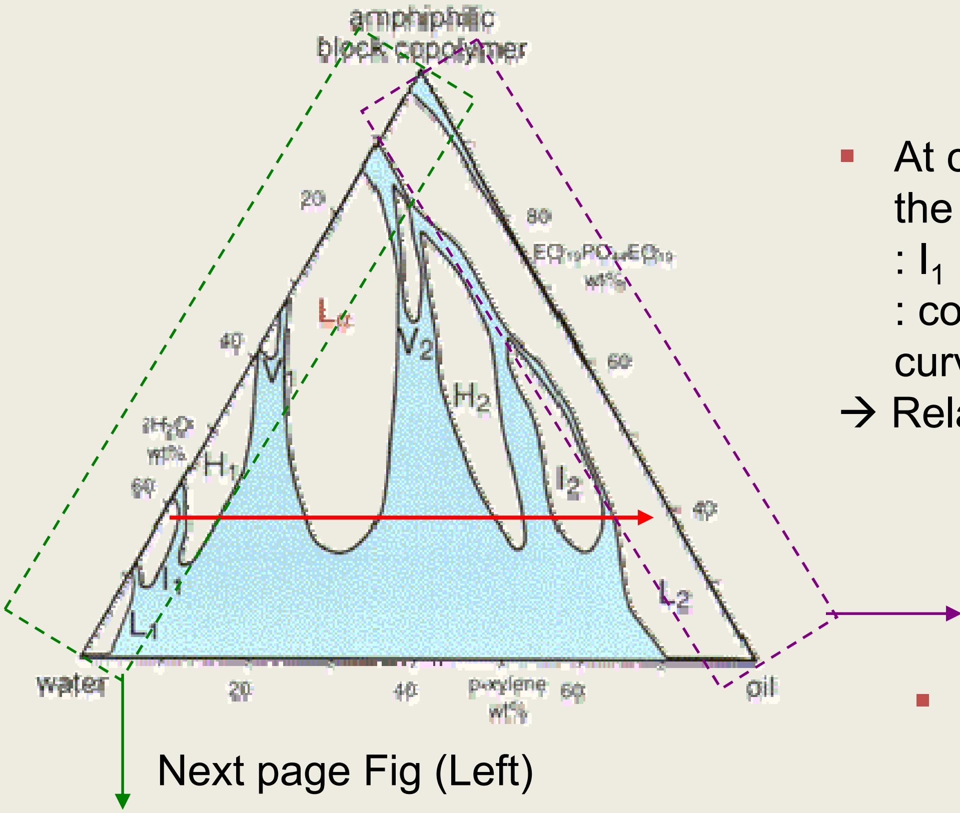
(2) Ternary amphiphilic block copolymer – water – oil system

- The lack of “mirror image” symmetry in the phase diagram → due to the different nature of the PEO-water and PPO-xylene interactions

Fig. Phase diagram of the $(EO)_{19}(PO)_{43}(EO)_{19}$ -H_2O- p-xylene ternary system.



(3) Progression of microstructure in block copolymer



Next page Fig (Left)

- At constant copolymer/oil ratio
  : $L_1 \rightarrow I_1 \rightarrow H_1 \rightarrow V_1 \rightarrow L_\alpha \rightarrow L_2$

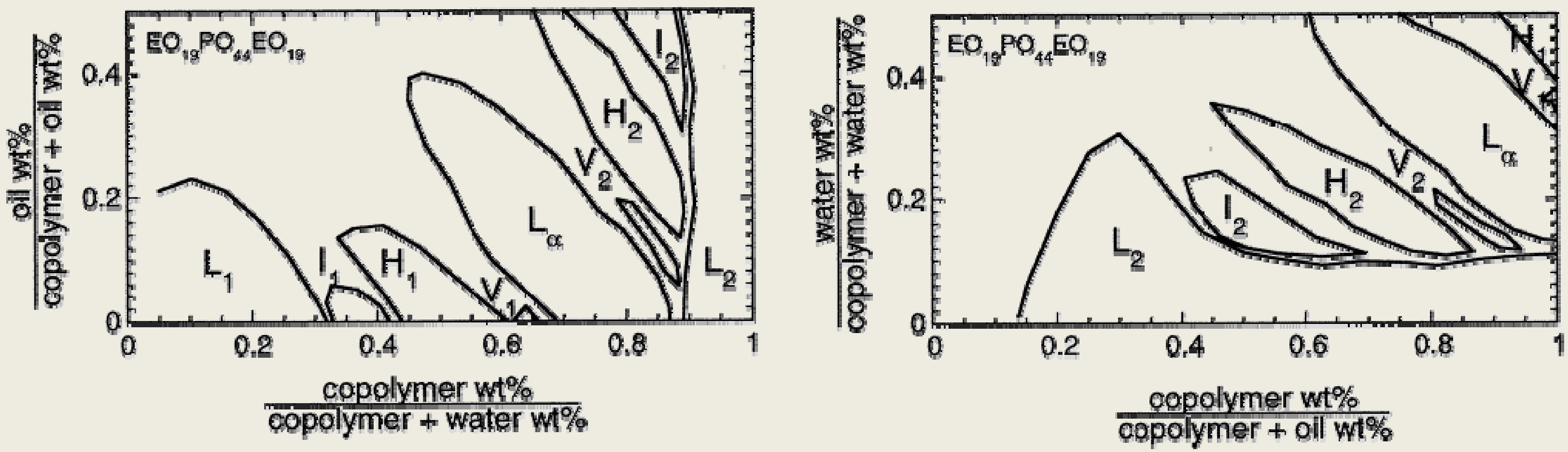
- At constant copolymer content (40 wt%), varying the water/oil ratio → phase changes
  : $I_1 \rightarrow H_1 \rightarrow L_\alpha \rightarrow H_2 \rightarrow I_2 \rightarrow L_2$ (⟶)
  : consistent with a decreasing interfacial mean curvature (H); H=0 in lamellar phase

→ Relates to geometric factor

Next page Fig (Right)

- At constant copolymer/water ratio

Fig. (Left) Boundaries of the various phases along the copolymer-water side of the ternary phase diagram (x-axis: copolymer weight fraction; y-axis: oil weight fraction). (Right) Boundaries of the various phases along the copolymer-oil side of the ternary phase diagram (x-axis: copolymer weight fraction; y-axis: water weight fraction).

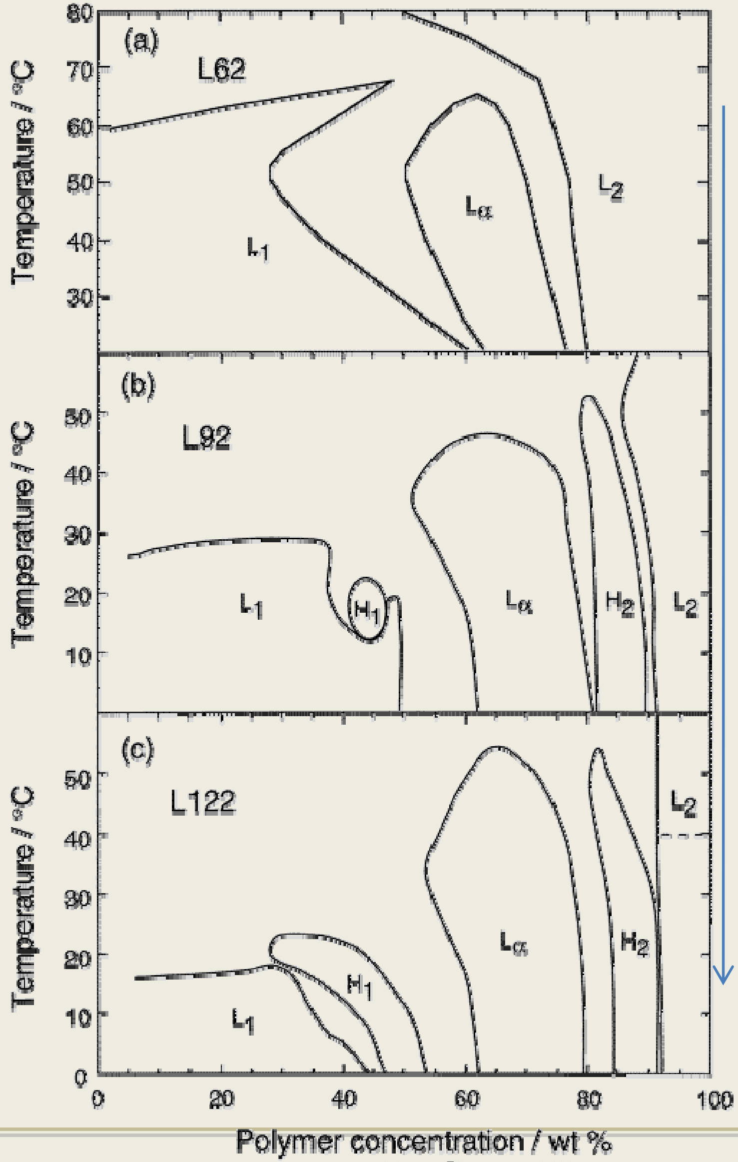


- For a PEO/PPO block copolymer of a given block composition and molecular weight, the types of structures appear to be a function of the volume fraction of the polar (water-like) / apolar (oil-like) components.
- The microstructure in such systems is not tied up to a specific block copolymer molecular weight and block composition, which define a point in the χN vs f phase diagram

3. A Closer Look at Microstructure

CNDL

(4) Effect of block copolymer molecular weight



- An increase in copolymer MW → increase the block segregation and the tendency for organization
- Figure confirms that a certain minimum MW is required for PEO and PPO blocks to segregate
  (a) only one mesophase L_α
  (b), (c) three mesophase and the increase of the range of the hexagonal regions when L92 → L122

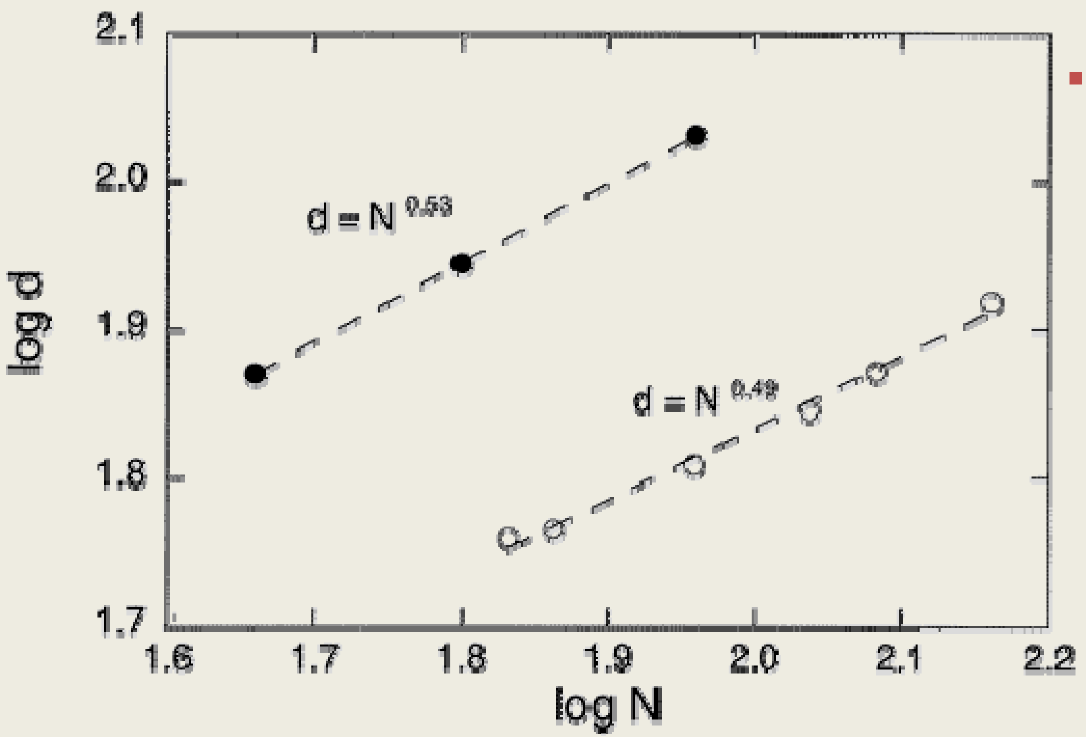
Increase in copolymer MW

Fig. Concentration-temperature phase diagrams for the (a) Pluronic L62/water, (b) Pluronic L92/water, and (c) Pluronic L122/water systems. L62, L92, and L122 have the same EO/PO ratio but different molecular weight (increasing in the order L62<L92<L122).

3. A Closer Look at Microstructure

- An important result from the study of MW affects concerns the dependence of the lamellar characteristic spacing on the polymer MW

Fig. Logarithm of the lamellar domain spacing d, vs the logarithm of number of polymer monomers N, for aqueous solution of Pluronic L62, L92, and L122 at 75 wt% (filled symbols) and calculated values from mean field theory (open symbols)



- $d \sim N^{1/2}$
  → characteristic of a random coil
  → the block copolymer chains are in the weak segregation regime

3. A Closer Look at Microstructure

(5) Effect of block copolymer composition

- The block composition is the main determinant of the microstructure observed in solvent-free block copolymers, and the chemical composition of typical surfactants affects their hydrophile/lipophile ratio and self-assembly properties.

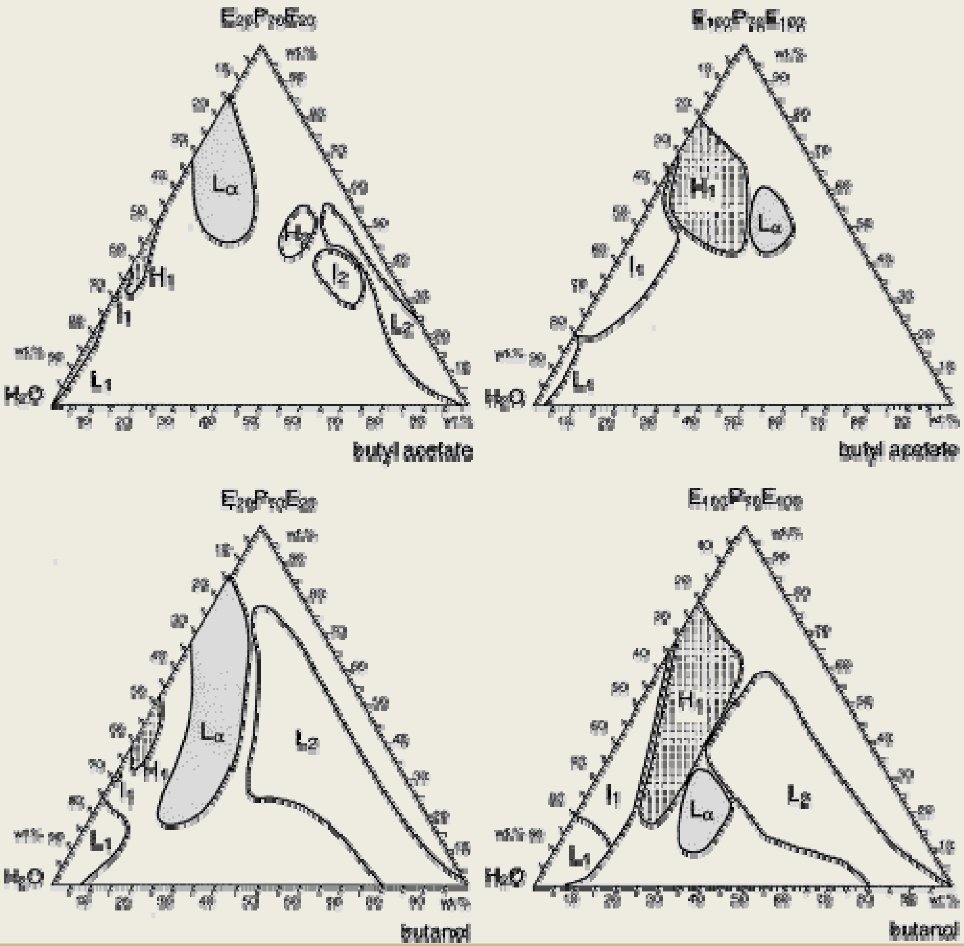
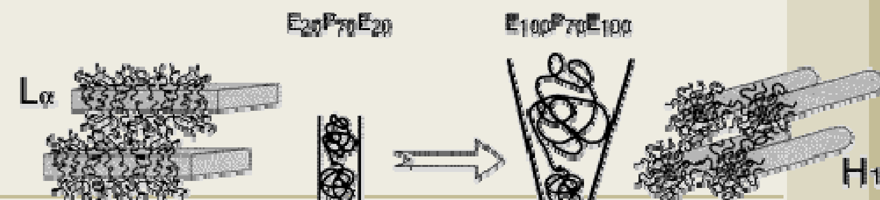


Fig. Phase diagrams of the copolymer-oil-water ternary systems.

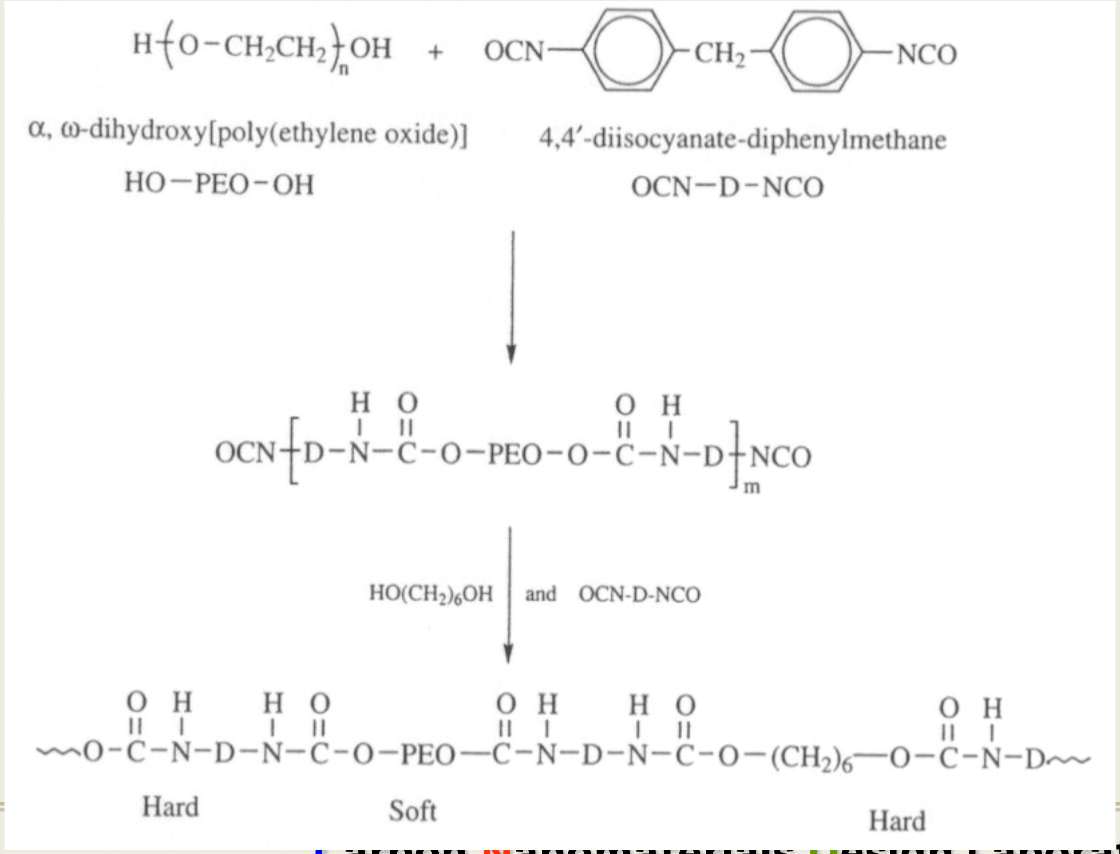
The change in phase behavior when
(i) the size of the copolymer E block changes from E_{20} to E_{100}
(ii) the "oil" changes from butyl acetate to butanol (top to bottom). The schematic represents the change of the self-organization of the amphiphilic block copolymers from the lamellar (L) to the normal hexagonal (H_1) structures upon an increase of the E block size and the corresponding increase in the interfacial curvature. The shaded areas represent the apolar domains.



4. Applications of Copolymers

4.1 Commercialized applications

- TPU (thermoplastic urethanes)
  → linear multiblock copolymer
  → the first commercially available TPE (thermoplastic elastomer)s which based on polyurethanes
  → automotive bumpers, snowmobile treads, etc.



Scheme.
General reactions scheme for the synthesis of TPU

4. Applications of Copolymers

- Kraton (Commercial name, Shell)

→ Linear triblock copolymer, made by anionic polymerization
→ Well-defined materials with low molecular weight and compositional heterogeneity
→ include footwear, bitumen modification, thermoplastic blending, adhesive, and cable insulation and gaskets.

- TPEs based on polyesters, TEPS (Commercial name, du Pont), and polyamides, TPA (Commercial name, Huls and Ato Chimie)

→Linear or polyamide multiblock copolymers
→Linked together by ester or amide linkage instead of urethane
→hose tubing, sport goods, automotive components, etc.

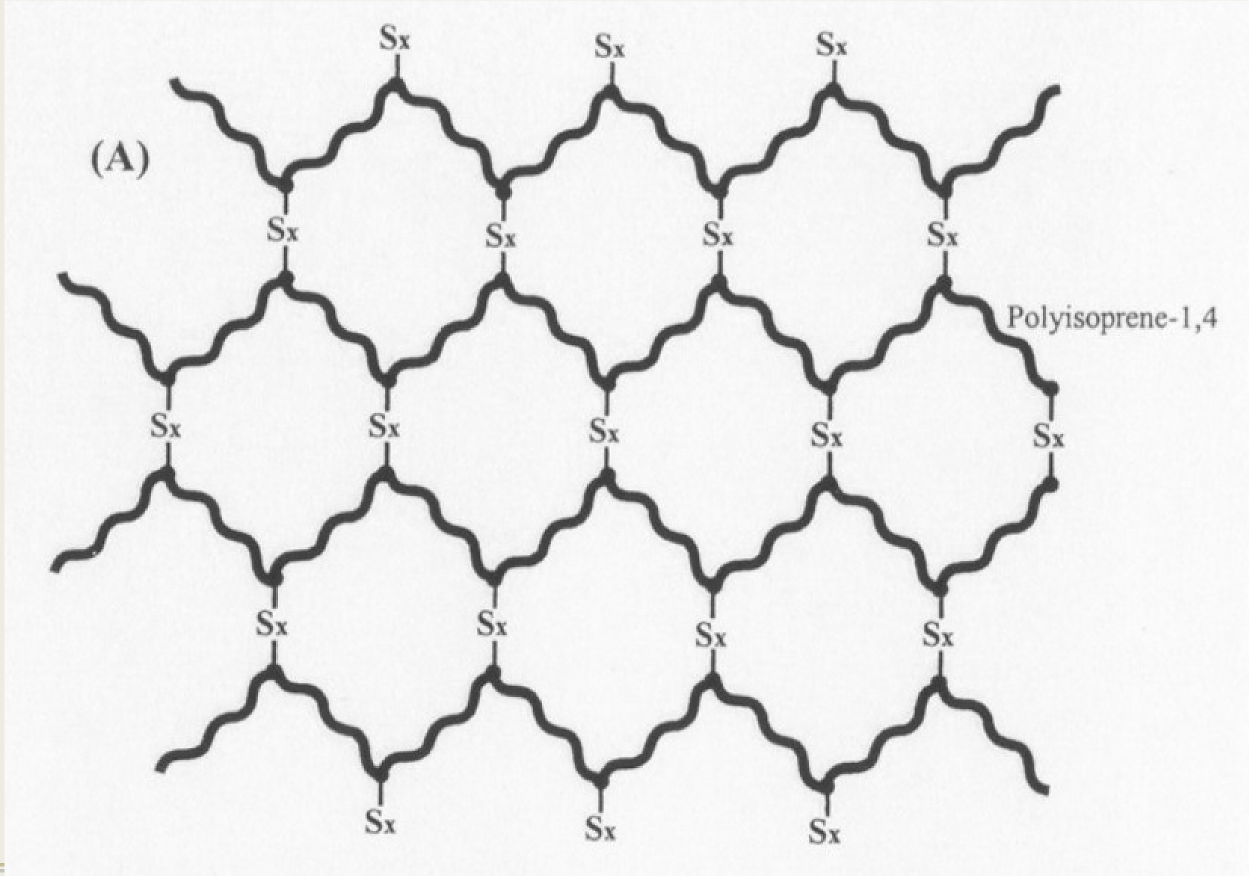
- All TPEs exhibit properties characteristic of chemically crosslinked elastomers at room temperature

→ At elevated temperature, behave as thermoplastics.
•They can be processed with high speed, efficiency and economy on conventional thermoplastic equipment.
•TPEs were considered to be one of the breakthroughs in rubber technology.

- On the molecular level,
  Thermoplasticity – consequence of noncrosslinked chains
  Thermoelasticity – consequence of crosslinked chains

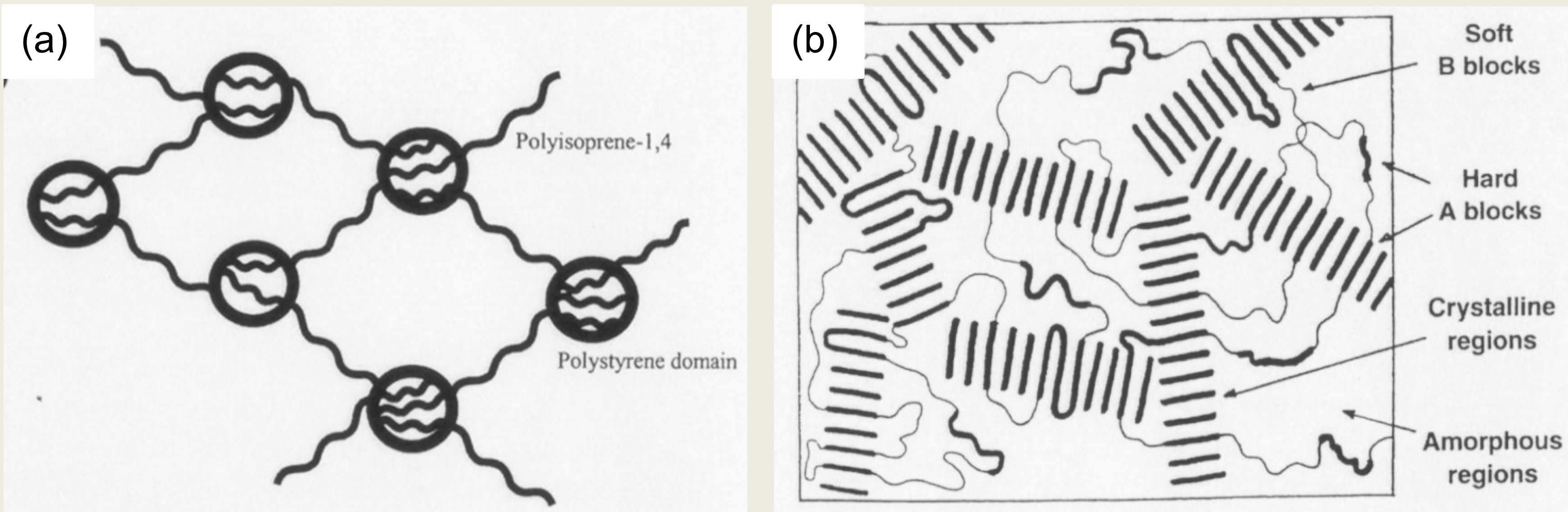
4. Applications of Copolymers

• In TPEs the crosslinks are physical rather than chemical, which is the case of vulcanized rubber.
• Thus, the hard domains lose their strength when the material is heated (thermoreversible) or dissolved in a solvent (solvoreversible).



4. Applications of Copolymers

• Thermoplastic elasticity is illustrated schematically for (a) styrenic TPEs and (b) multiblock TPEs.



• Crystallinity (TPES, TPA), hydrogen bonding (TPU,TPA), and van der Waals interactions (styrenic) all have been shown to cause microphase separation in these systems.

4. Applications of Copolymers

• Triblock copolymers with polydienes end blocks and diblock copolymers are not TPEs because the flexible chains are not immobilized at both ends by the glassy hard domains of PS and, consequently, cannot be elastic.

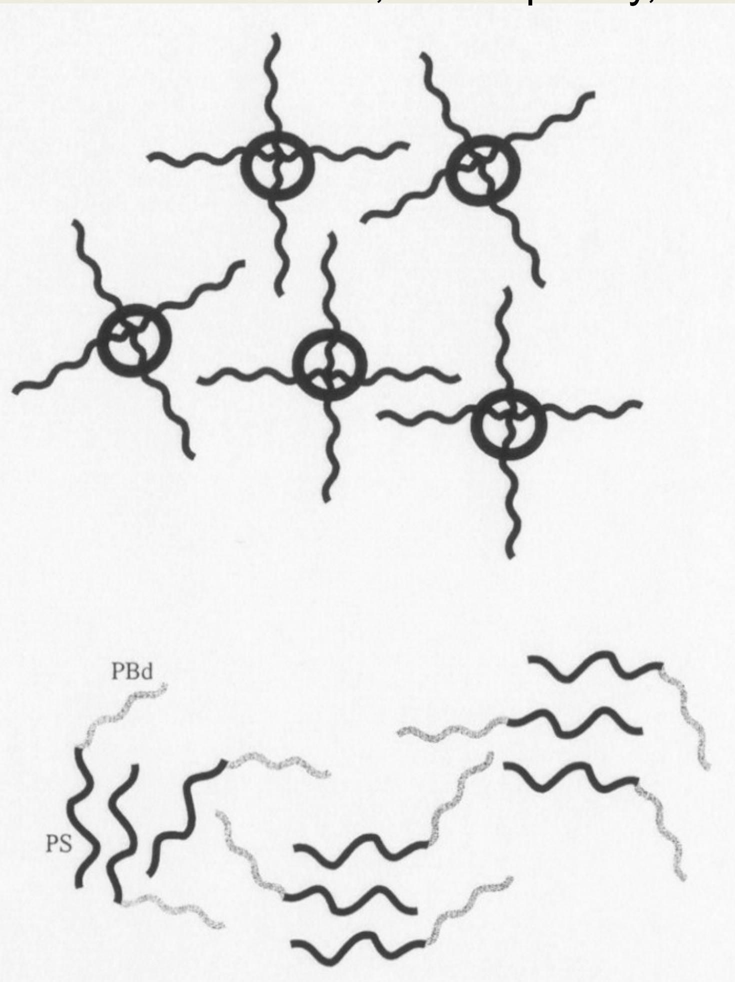
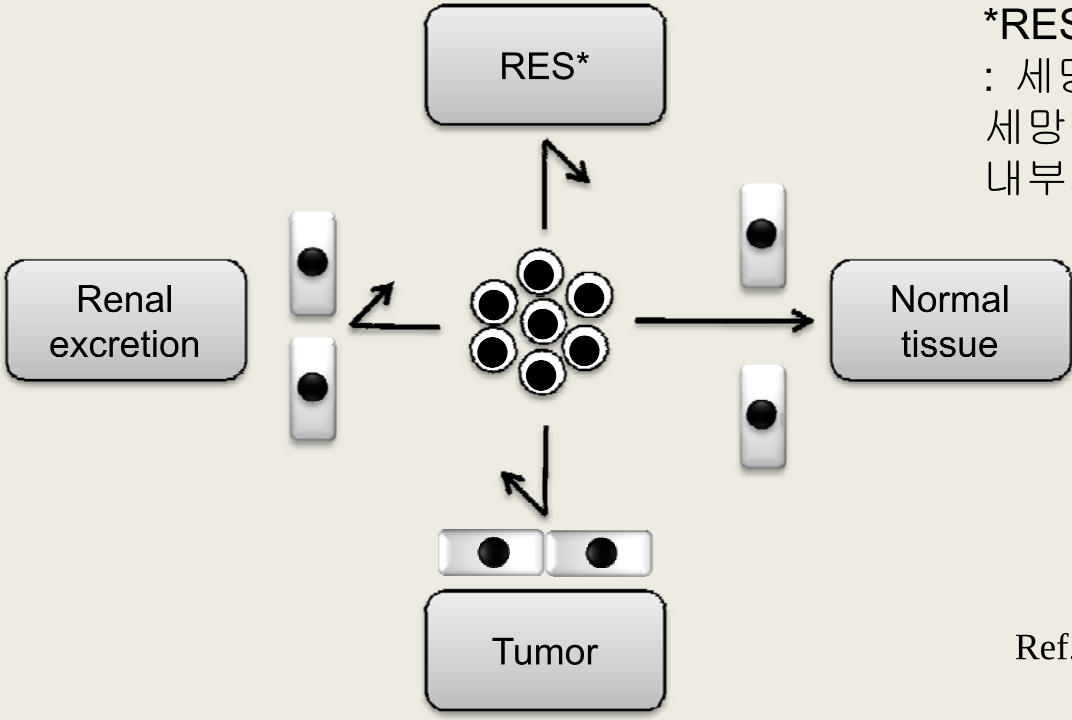


Fig. Styrenic triblock copolymer with polydiene external block or diblock copolymers (styrene or PU) are not elastic.

4.2 Potential Applications

(1) Drug release in target cells

- A block copolymer for use in drug delivery as a microcontainer device must consist of a water-soluble block(hydrophilic), in order to impart blood solubility of the microcontainer, and a water-insoluble block (hydrophobic) compatible with the drug to be carried.



*RES (reticuloendothelial system)
: 세망내피계 (림프절 지라 골수 등 속의 세망세포나 간 부신(副腎) 등 특별한 기관 내부의 혈관 내피세포 등의 총칭)

Fig. Accumulation of micelle-forming microcapsules in a tumor utilizing enhanced permeability of tumor vasculature

Ref. *Macromol. Symp.* (1997) **118**, 577.

4. Applications of Copolymers

(2) Nanopatterning

- Sizes less than 30nm are not easily obtained standard lithography (photolithography, electron beam lithography).
- One way to overcome this problem is by using block copolymer

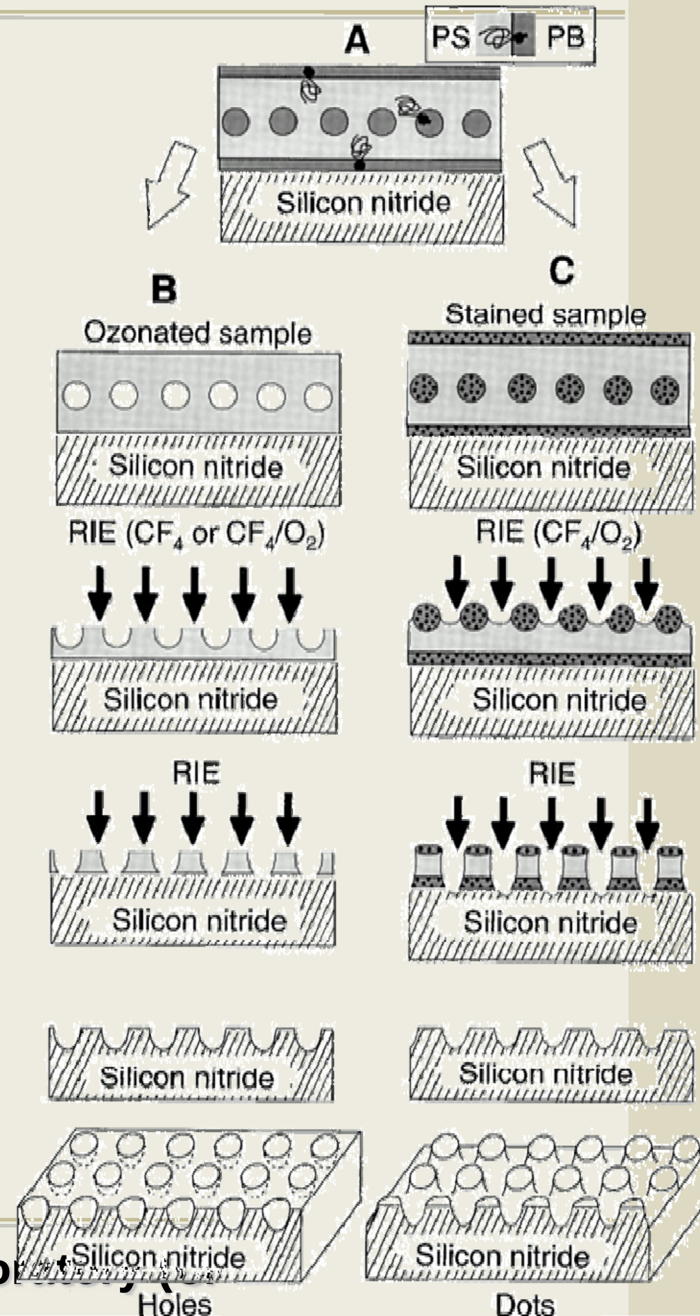


Fig. (A) Schematic cross-sectional view of a nanolithography template consisting of a uniform monolayer of PB spherical microdomains on silicon nitride. PB wets the air and substrate interfaces. (B) Schematic of the processing flow when an ozonated copolymer film is used, which produces holes in silicon nitride. (C) Schematic of the processing flow when an osmium-stained copolymer film is used, which produces dots in silicon nitride.

Ref. *Science* **276** (1997) 1401

4. Applications of Copolymers

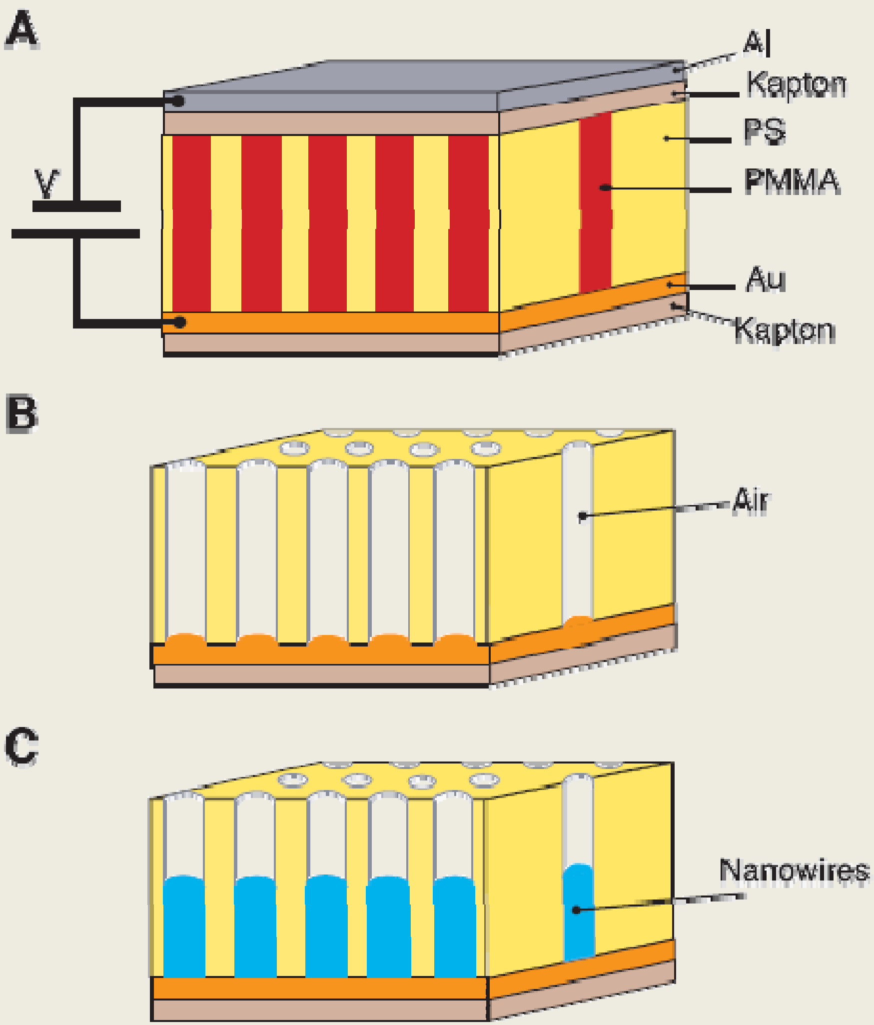


Fig. A schematic representation of high density nanowire fabrication in a polymer matrix.
(**A**) An asymmetric diblock copolymer annealed above the glass transition temperature of the copolymer between two electrodes under an applied electric field, forming a hexagonal array of cylinders oriented normal to the
film surface. (**B**) After removal of the minor component, a nanoporous film is formed. (**C**) By electrode position, nanowires can be grown in the porous template, forming an array of nanowires in a polymer matrix.

Ref. *Science* **290** (2000) 2126.

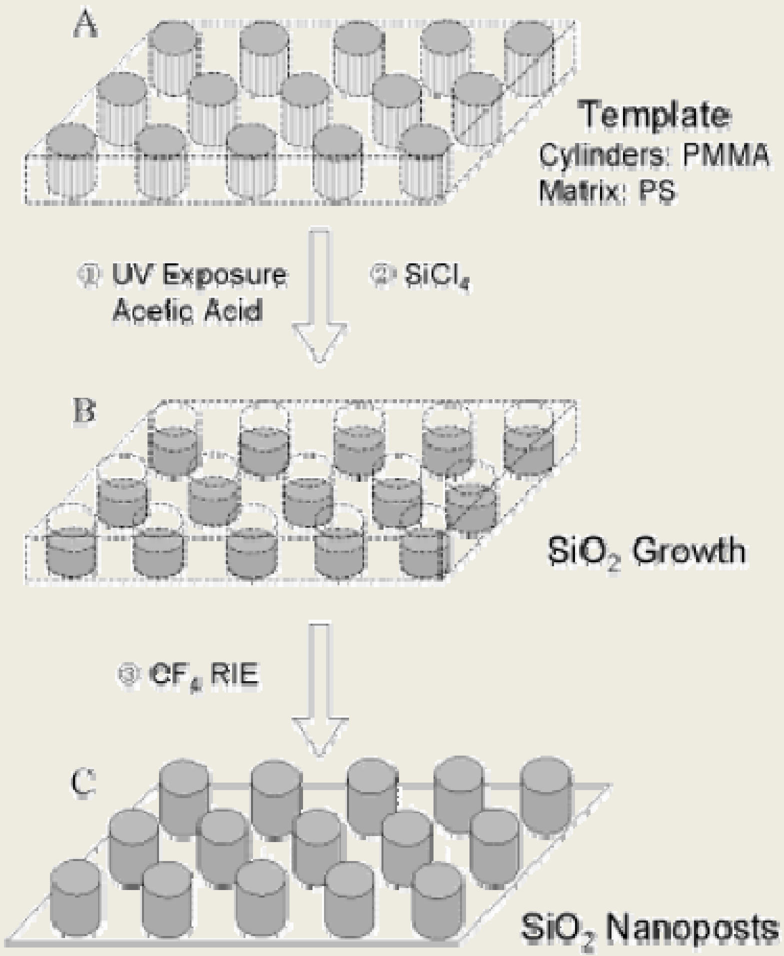


Fig. Schematic diagram of the steps required to generate SiO_2 nanoposts. A) Block copolymer films having cylindrical microdomains oriented normal to the surface. B) Growth of SiO_2 within the nanopores generated by selective elimination of PMMA cylinders. C) Array of SiO_2 nanoposts after removing PS matrix with CF_4 RIE.

Ref. *Adv. Mater.* **13** (2001) 795.

4. Applications of Copolymers

(3) Organic-inorganic hybrid mesostructures

- By using an amphiphilic block copolymer as a structure-directing agent, organic-inorganic hybrid materials with nanoscale structures can be prepared.

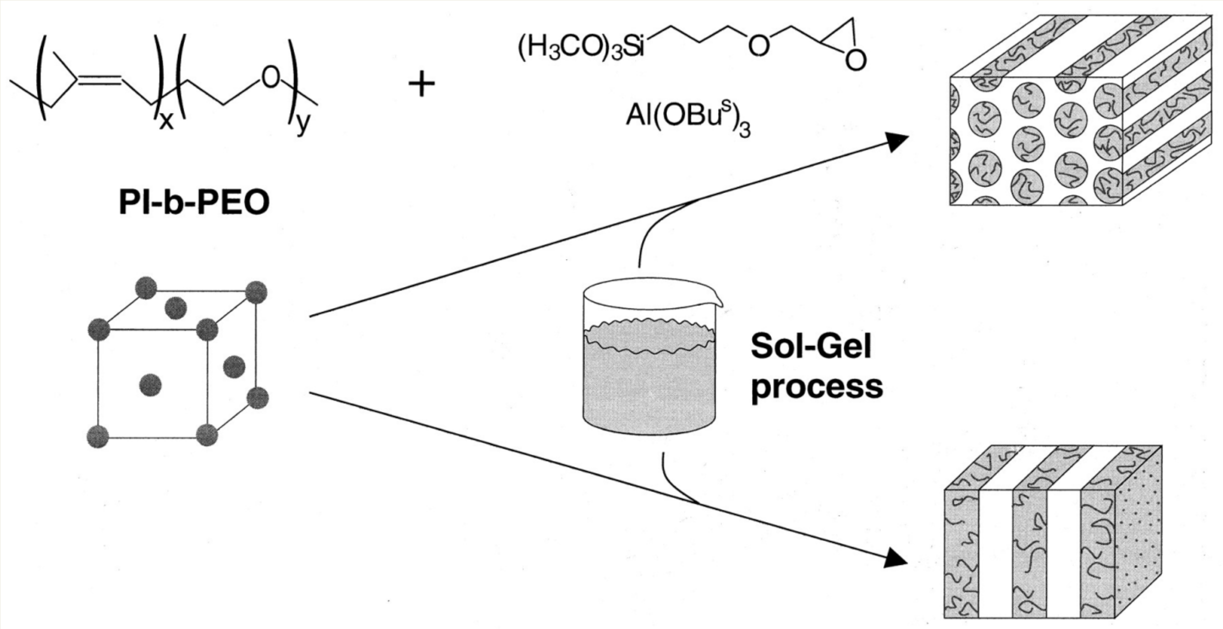


Fig. Schematic drawing of our approach for synthesizing organically modified silica mesostructures.

Ref. *Science* **278** (1997) 1795.

CNDL

- By thermal treatment, single ceramic nanoobjects of different shapes and sizes can be prepared.

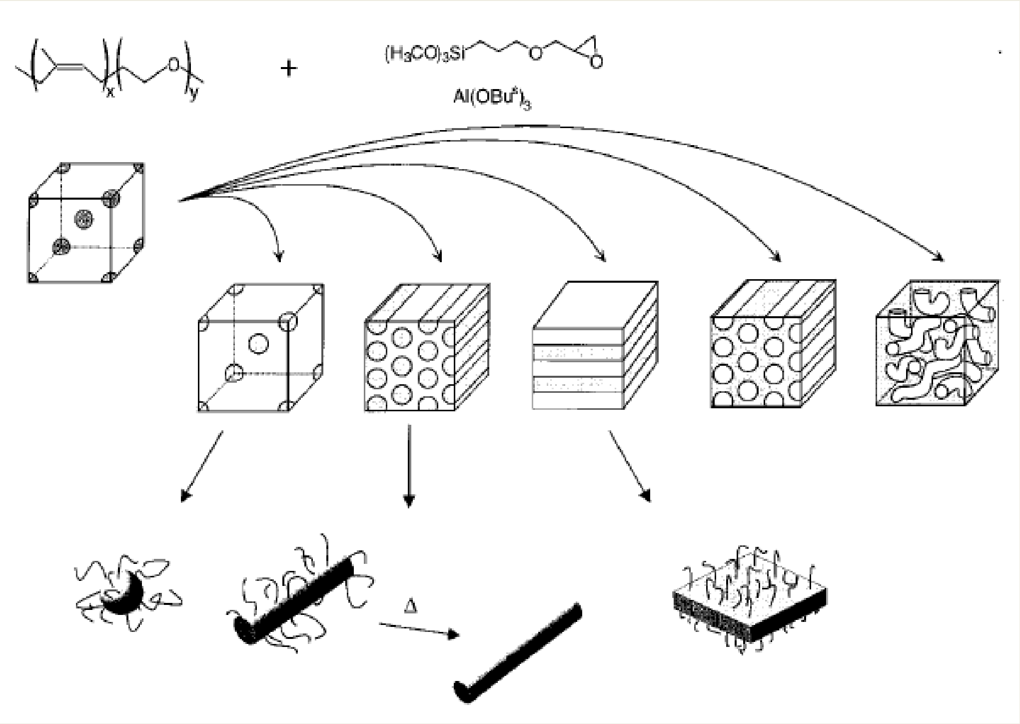


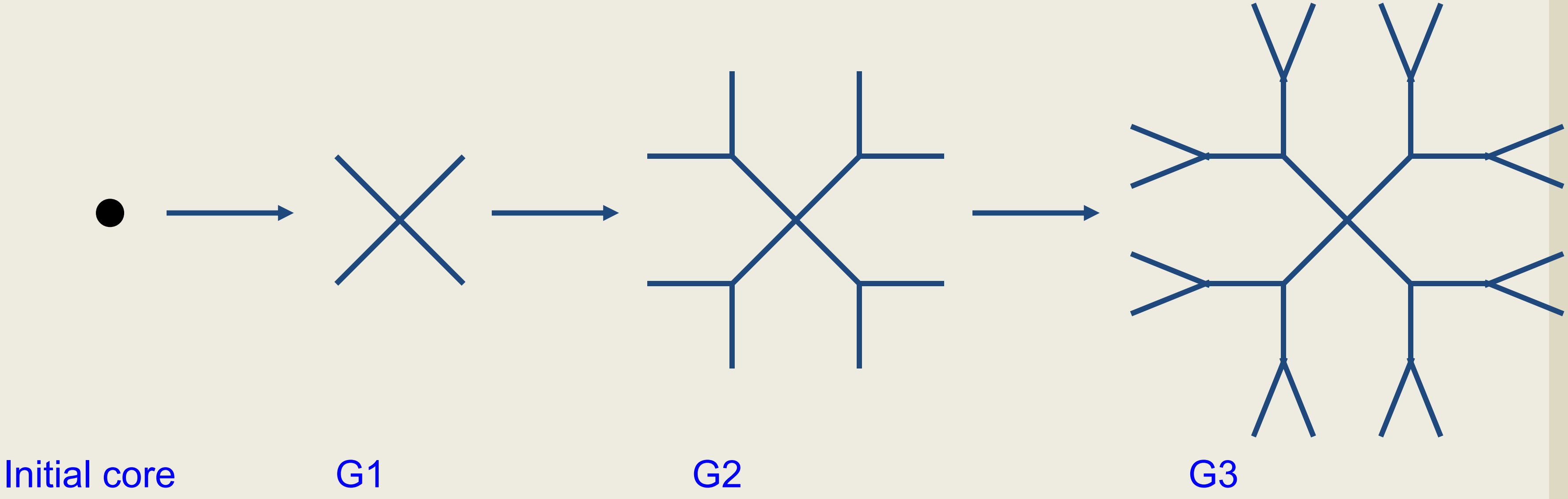
Fig. Schematic drawing of our approach for synthesis of single nano-objects with controlled shape, size, and composition. In the upper part all morphologies obtained from PI-b-PEO and different amounts of metal alkoxides are shown. As displayed in the lower part of the figure, the single “hairy” hybrid nano-objects of different shape are isolated by dissolution.

2.1.2.2. Dendrimer, DNA

1. **What Are Dendrimers?**
   - 1.1. Definition of Dendrimers
   - 1.2. The Structure of Dendrimers
   - 1.3. Examples of Dendrimers
2. **Dendrimer Construction Strategies**
   - 2.1. Divergent Approach
   - 2.2. Convergent Approach
   - 2.3. Cores & Branching units
3. **The Ideas for Finding Applications of Dendrimers**
   - 3.1. Functionalized Dendrimers
   - 3.2. Host-Guest Chemistry with Dendrimers
   - 3.3. Dendritic Micelles
   - 3.4. Dendrimers in Drug Delivery System
4. **Introduction of DNA**
   - 4.1. What is DNA?
   - 4.2. Structure of DNA
   - 4.3. Chemical synthesis of DNA
   - 4.4. DNA hybridization
5. **Self-assembled nanostrucutres based on DNA**
   - 5.1. DNA-directed assembly of proteins
   - 5.2. Organization of inorganic nanoclusters
   - 5.3. DNA-templated synthesis

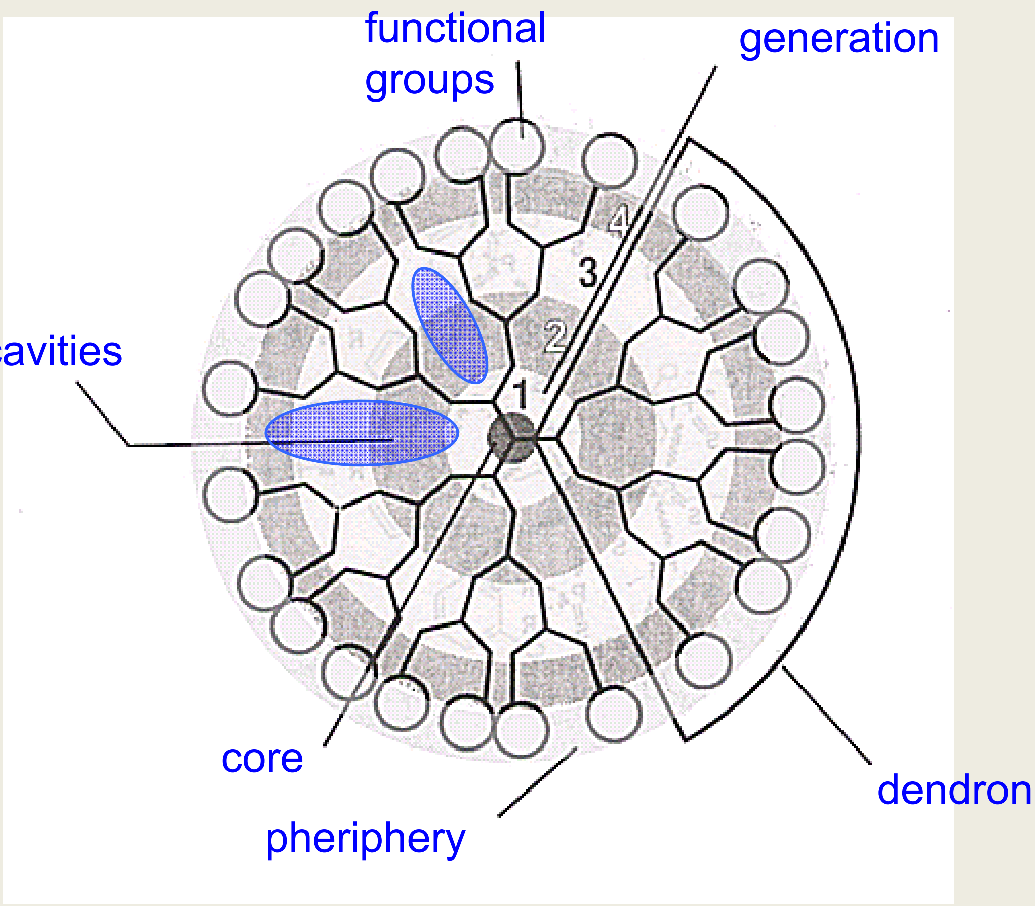
1.1 Definition of Dendrimers

; Evolving around a core atom or molecule, they possess repeating “generations” of branch again and again until an almost globular shape with a dense surface is reached.



CNDL

1.2 The Structure of Dendrimers



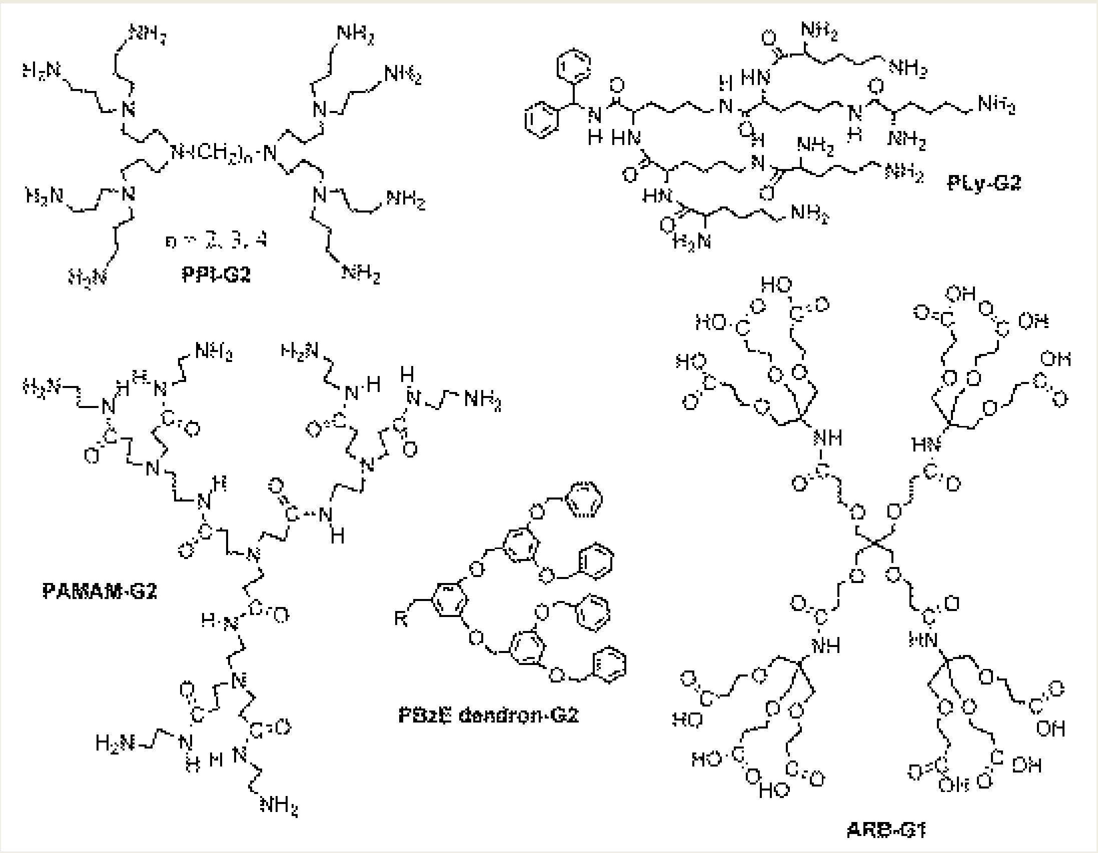
; Nano-sized spherical shape

; Low polydispersity

; Pheriphery - polyfunctionality

; Cavity (vacant space)
- possible to use as drug carrier

1.3 Examples of dendrimers



PPI, Poly(propylene)imine

Ply, Polylysine

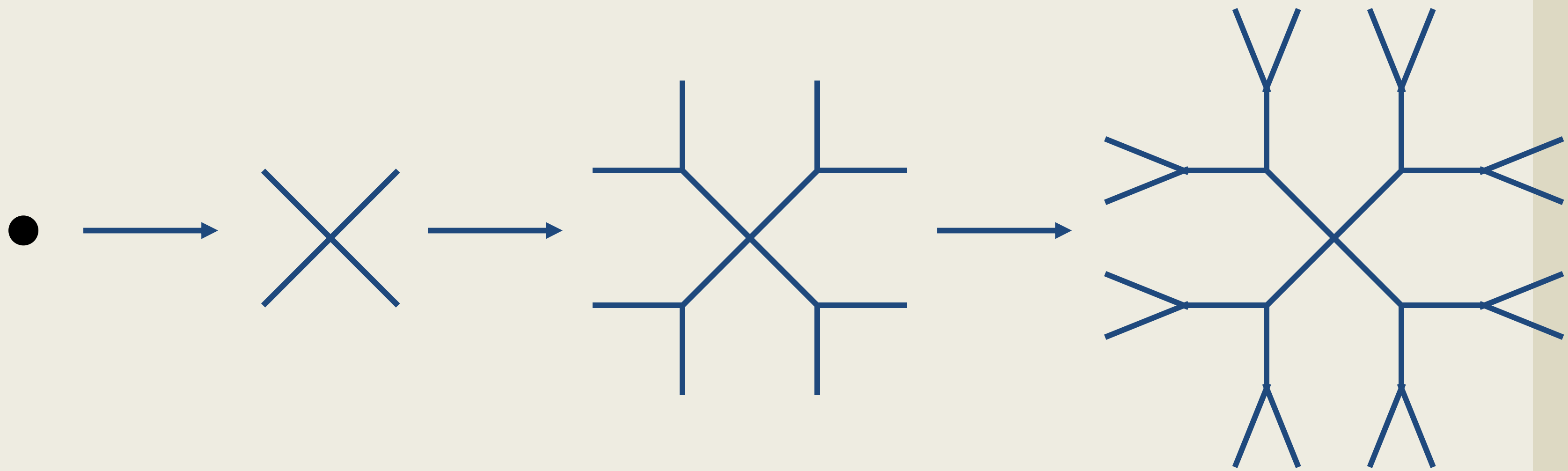
PAMAM, poly(amidoamine)

ARB, arborol

PBzE, poly(benzyl ether)

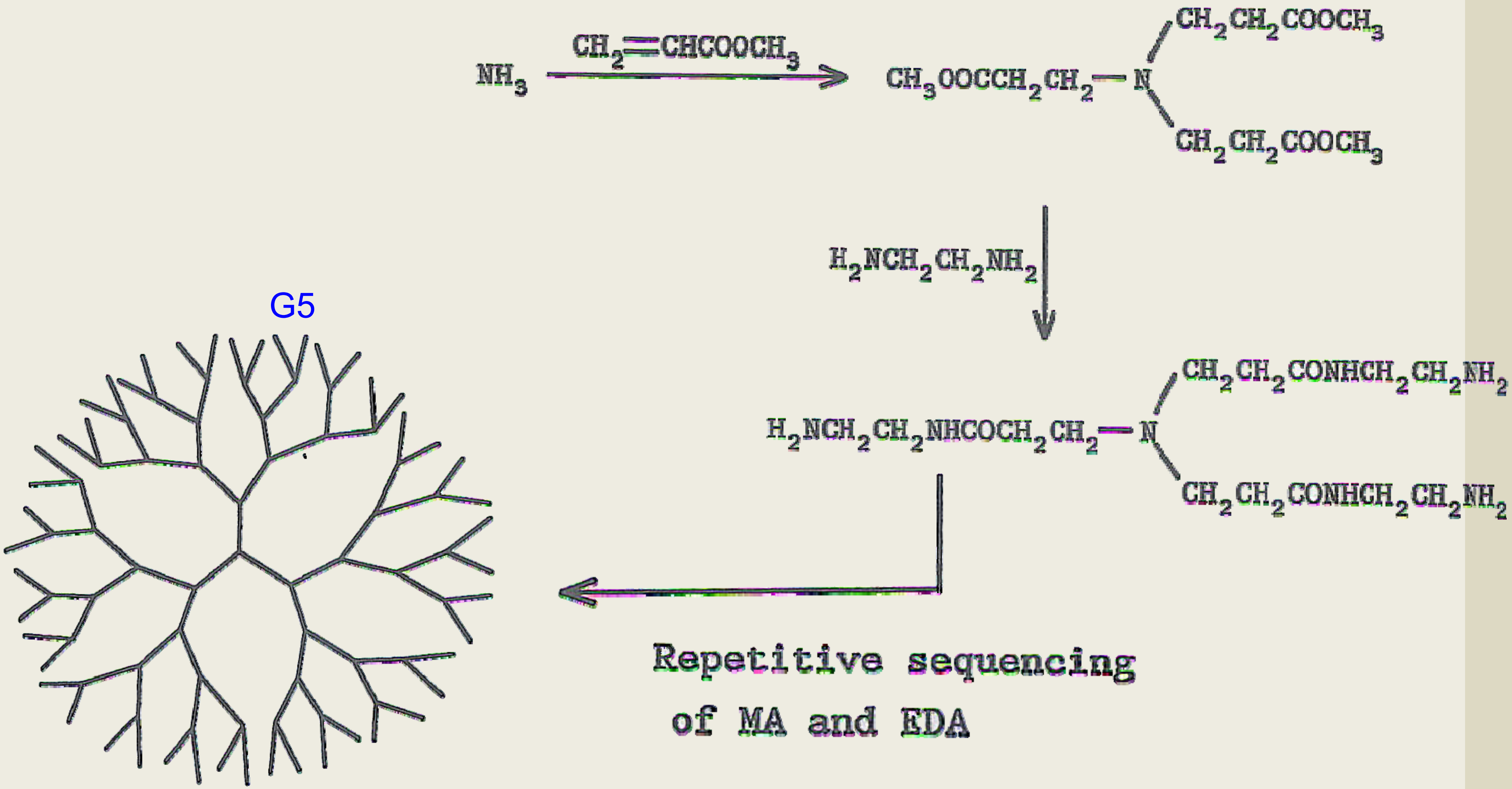
2.1 Divergent Approach (core to periphery)

; The divergent method starts with a core moeclue and builds outward by attaching to the core successive layers (or generations) of monomer units one at a time.



2. Dendrimer Construction Strategies

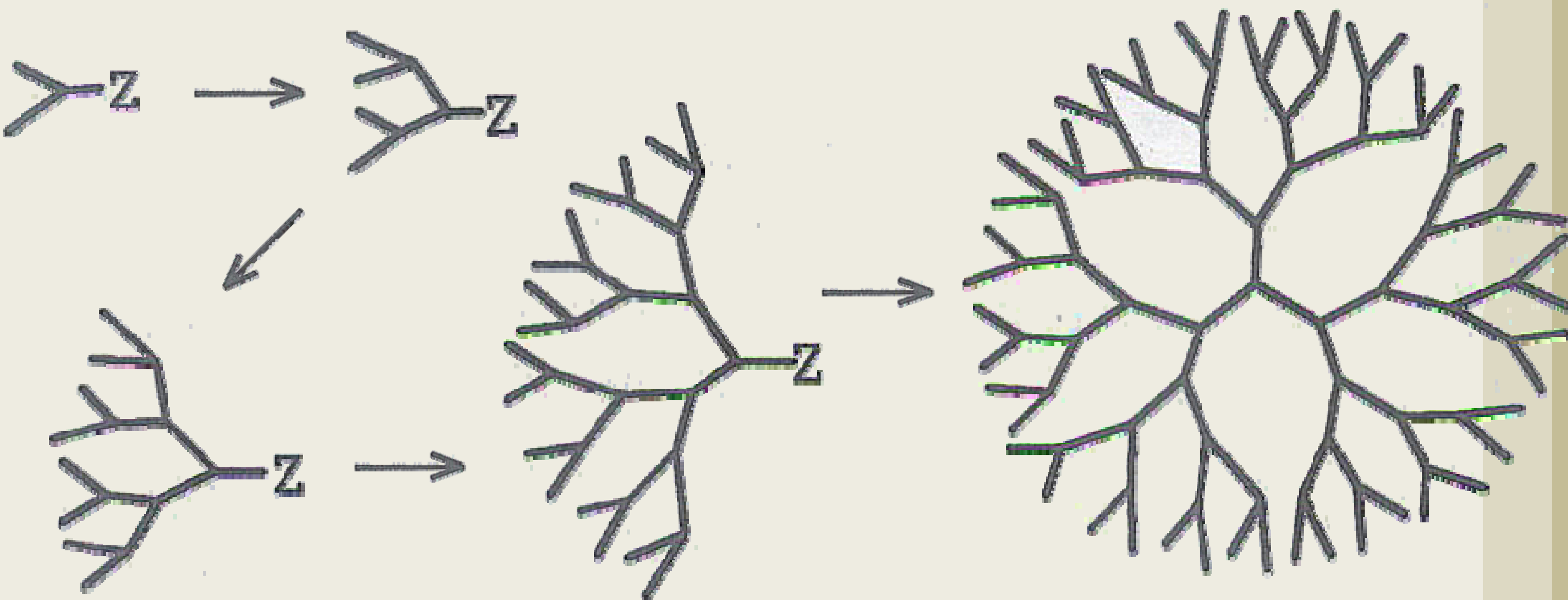
✓ Divergent synthesis of PAMAM dendrimer



Ref. “Principle of Polymerization” 4th Ed, Hoboken, N.J. : Wiley, 2004

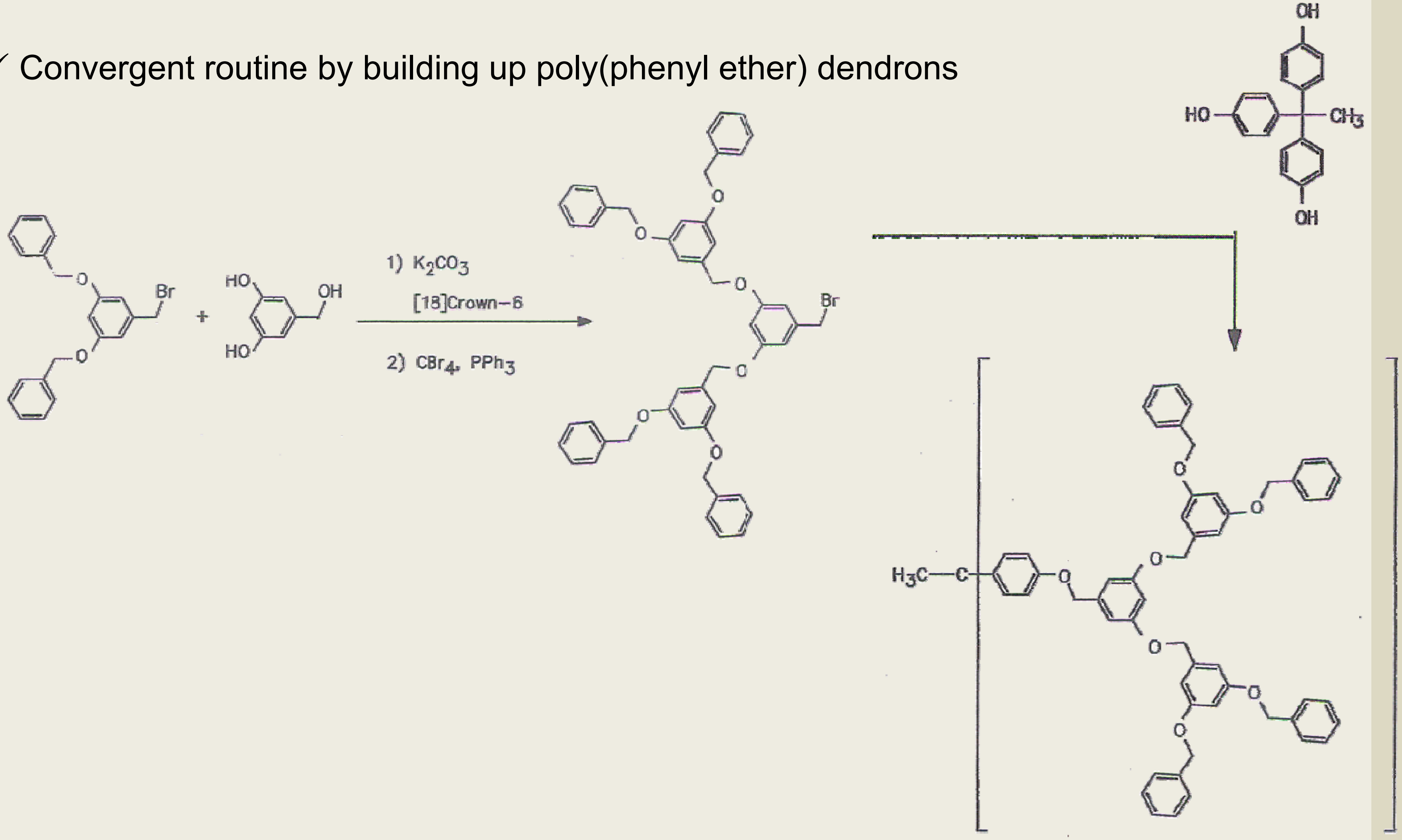
2.2 Convergent Approach

; Dendrimeric fragments are synthesized by repetitive reactions, and then several are joined together in the last step by using a central core molecule to form the dendrimer.



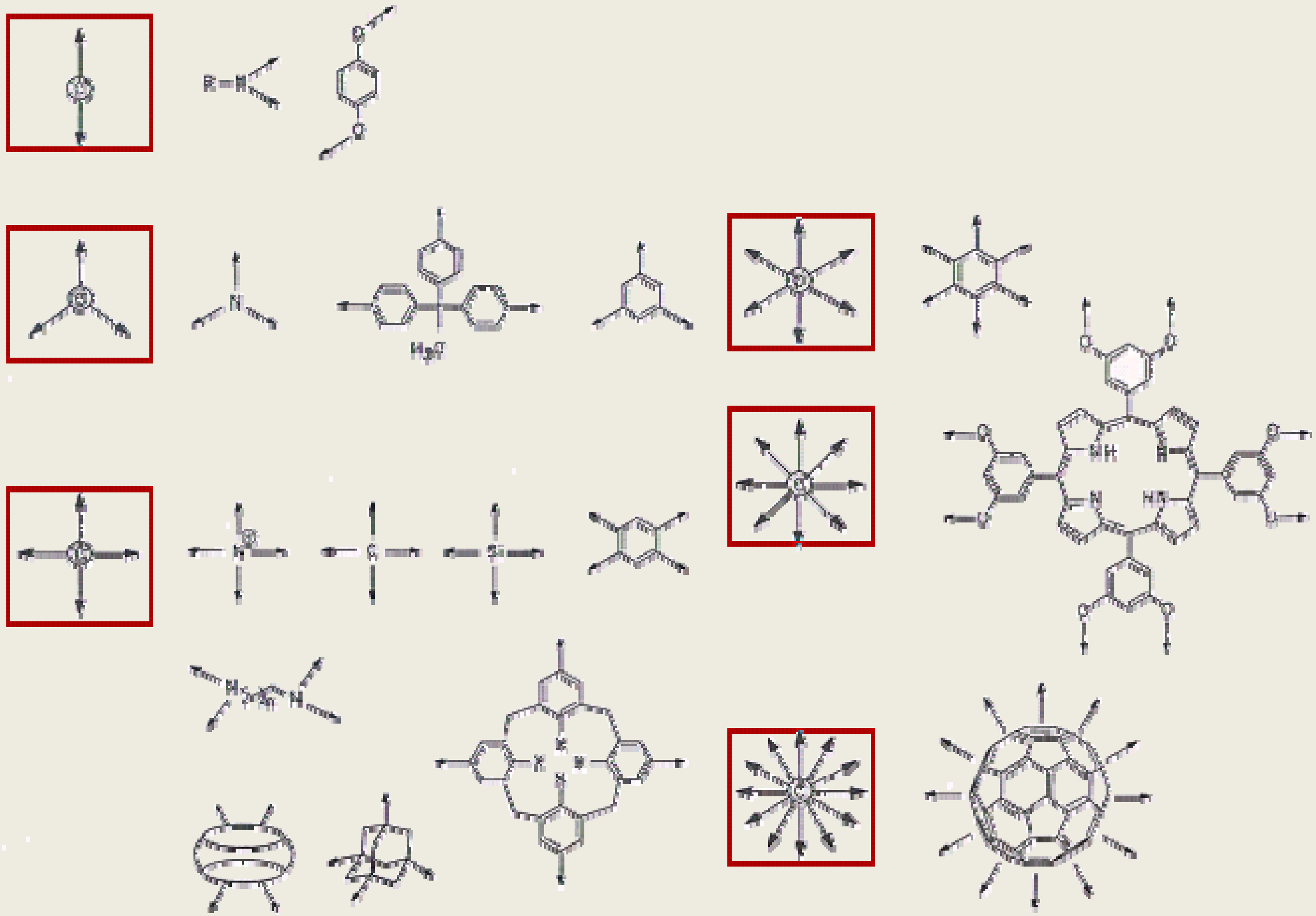
2. Dendrimer Construction Strategies

✓ Convergent routine by building up poly(phenyl ether) dendrons



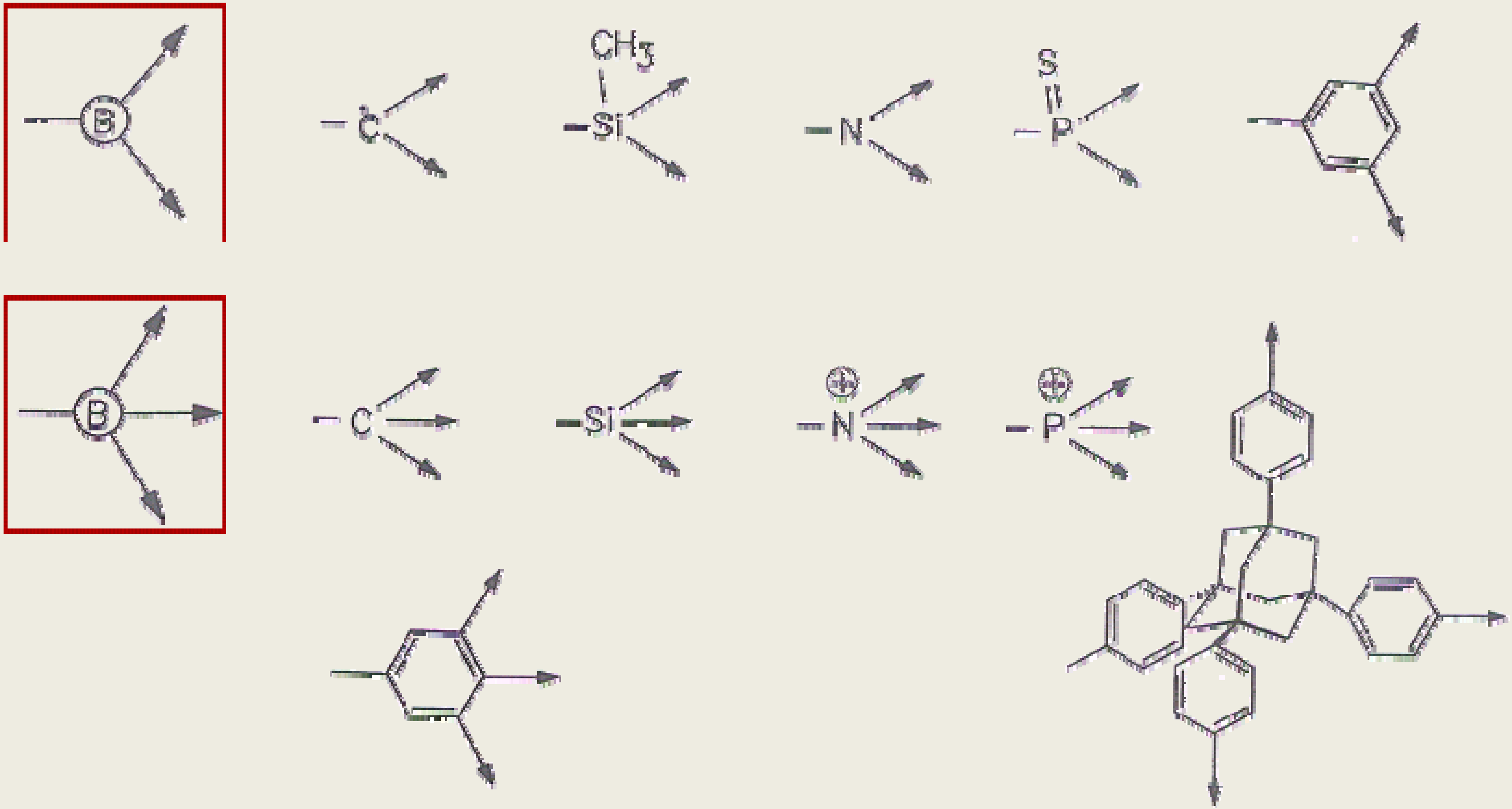
2.3 Cores & Branching units for building up the dendrimer

- ✓ Cores

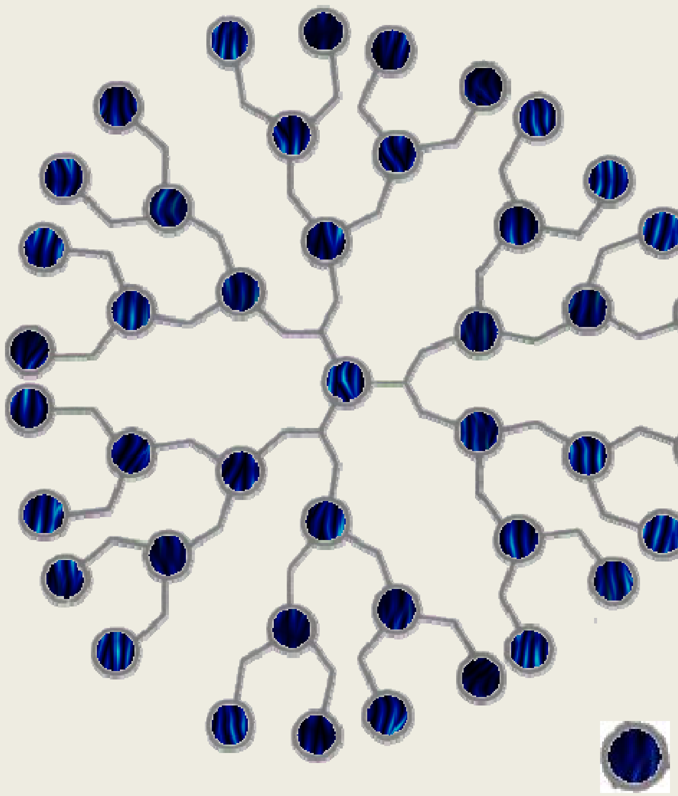


2. Dendrimer Construction Strategies

✓ Branching units



3.1 Functionalized Dendrimers



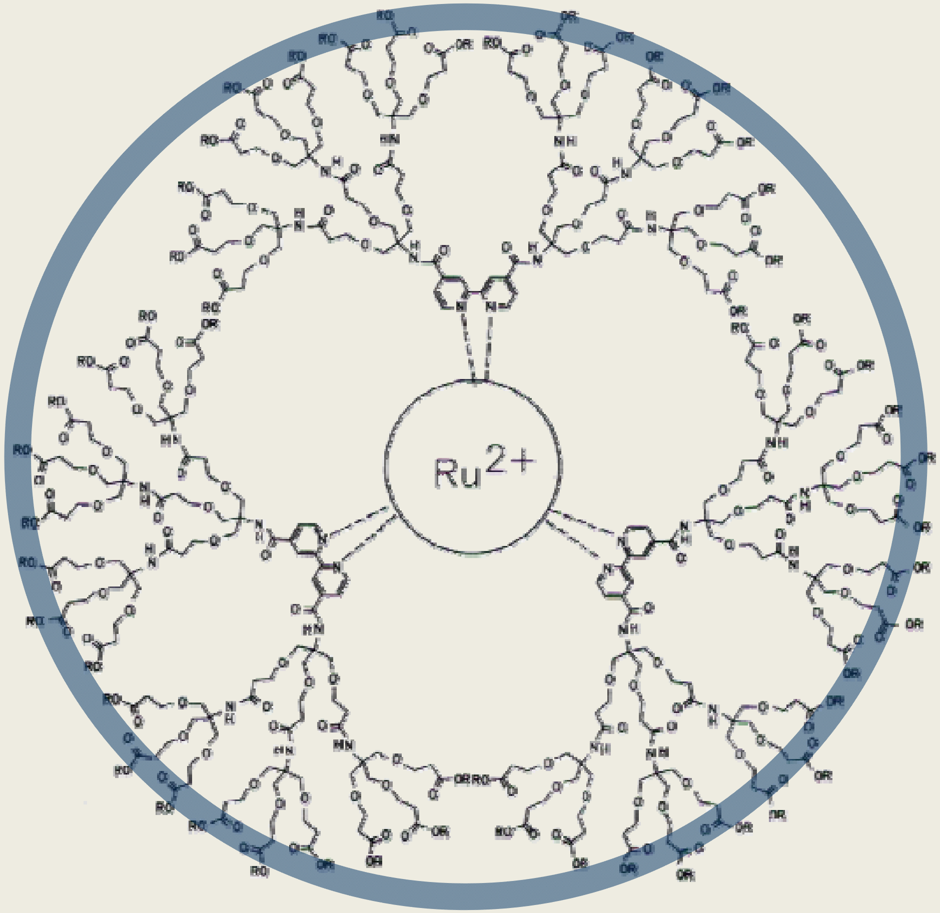
Core, branches, periphery

; Introduction of functional group to dendrimers

; The kind of sites in dendrimer molecues can be functionalized.
→ core, branch, periphery

; A lot of functional groups can be introduced to dendrimer molecules.

✓ Metal-functionalized dendrimers



; Ru^{2+} can be applied in medical diagonostics.

; Ru^{2+} can be quenched by solvent or with dissolved oxygen.

Ru^{2+} + Sol(solvent) → Ru-Sol complex

$Ru^{2+} + O_2 \rightarrow RuO_4$

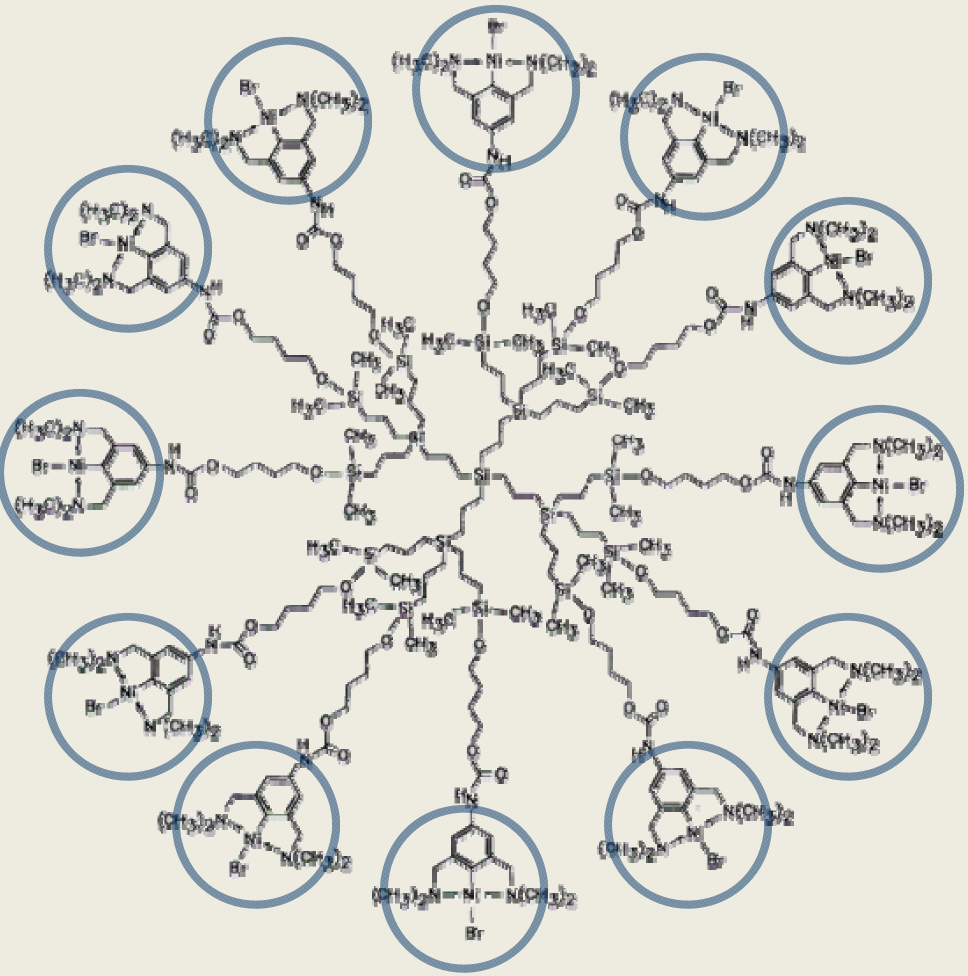
; Dendrons can serve as shields for Ru^{2+} (Shielding effect)

→ Prevent quenching processes with the solvent or with dissolved oxygen

→ Increase of lifetime of the excited state of Ru^{2+}

3. The Ideas for Finding Applications of Dendrimers

✓ Metal-functionalized dendrimers

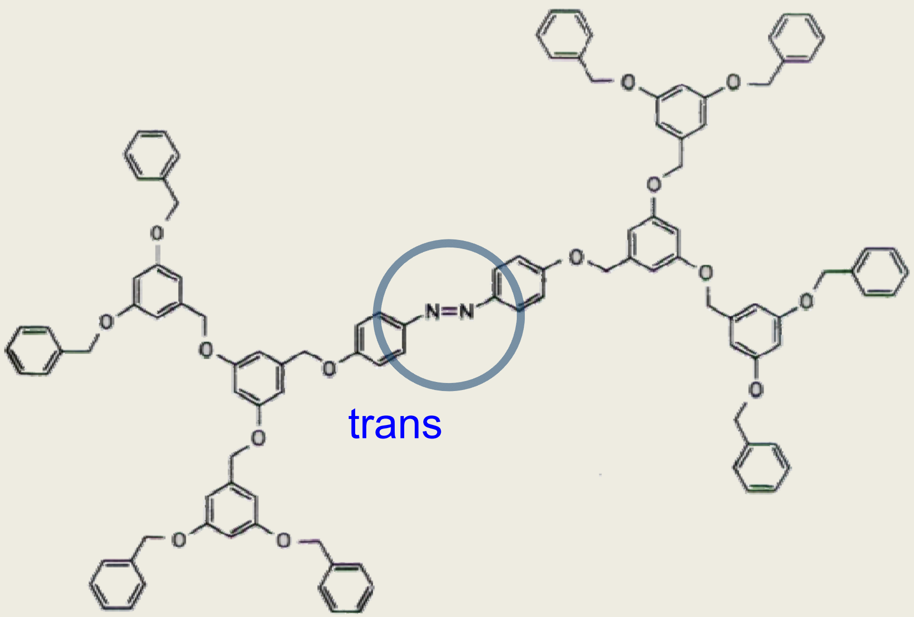


; periphery-functionalized dendrimer by aryl nickel (catalyst)

; In a molecule, a lot of aryl nickels are contained.
→ can be used for new kind of catalyst
→ “Dendralyst”

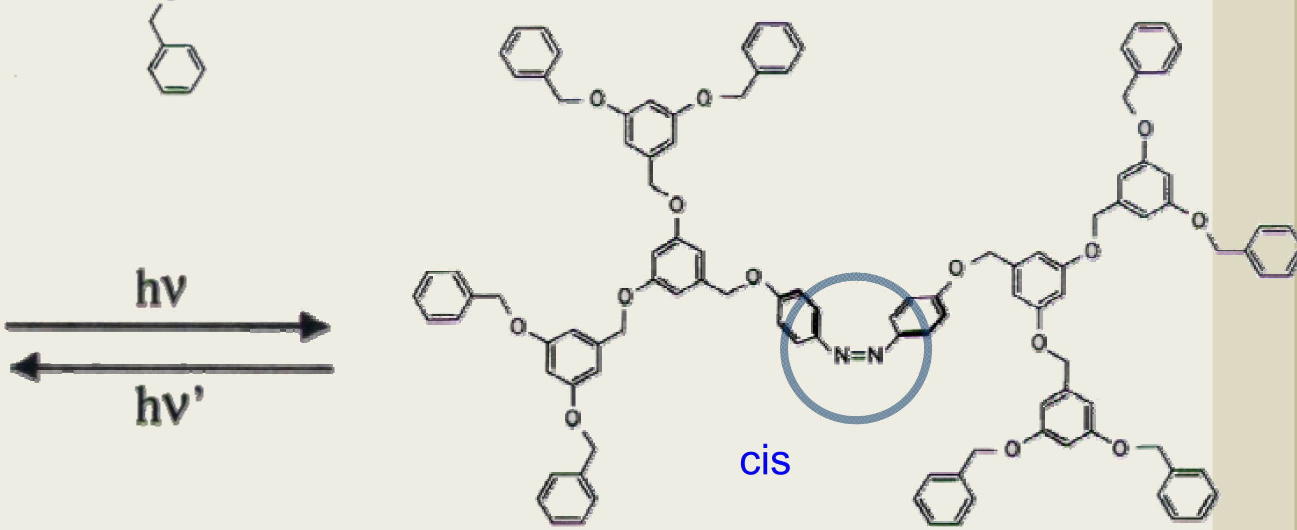
; As varied the kind of metal, different electrochemical properties can be introduced to dendrimers.

✓ Photoactive azobenzene dendrimers

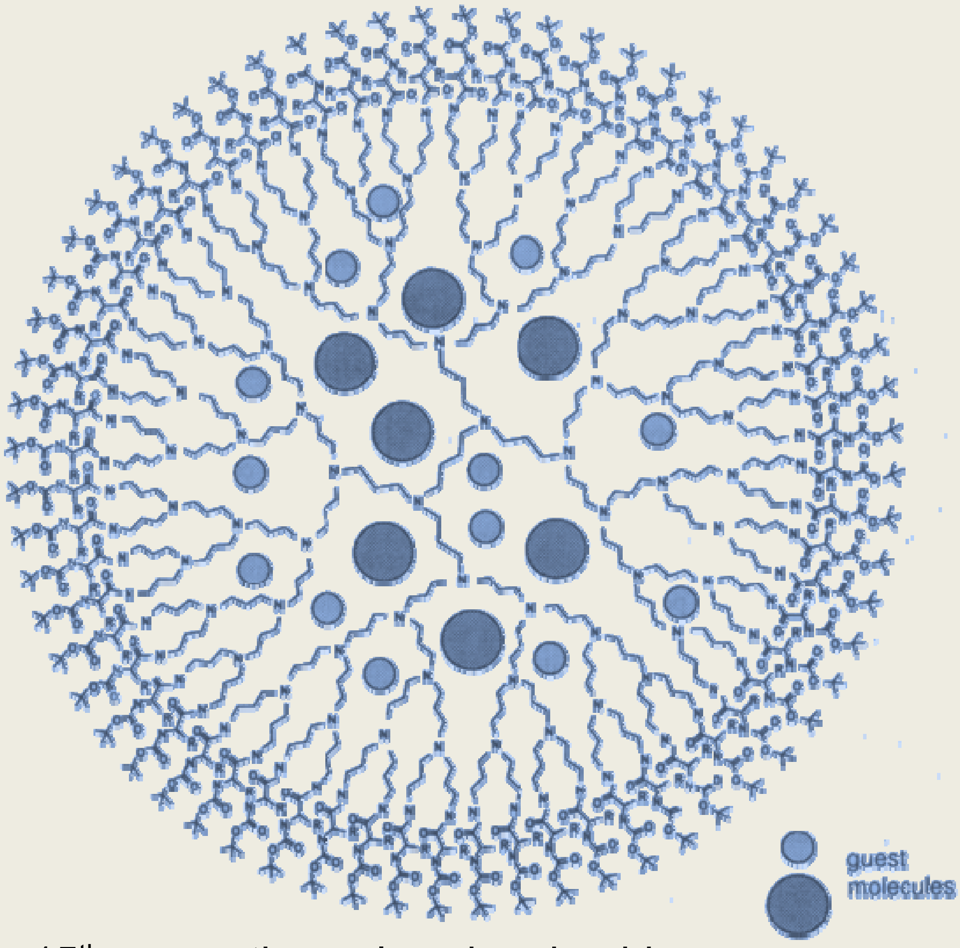


; core-functionalized by azo compound

; Azo-type compounds can be easily and reversibly photoisomerized.
→ Photoresponsive molecule



3.2 Host-Guest Chemistry with Dendrimers



15th-generation polyamine dendrimer

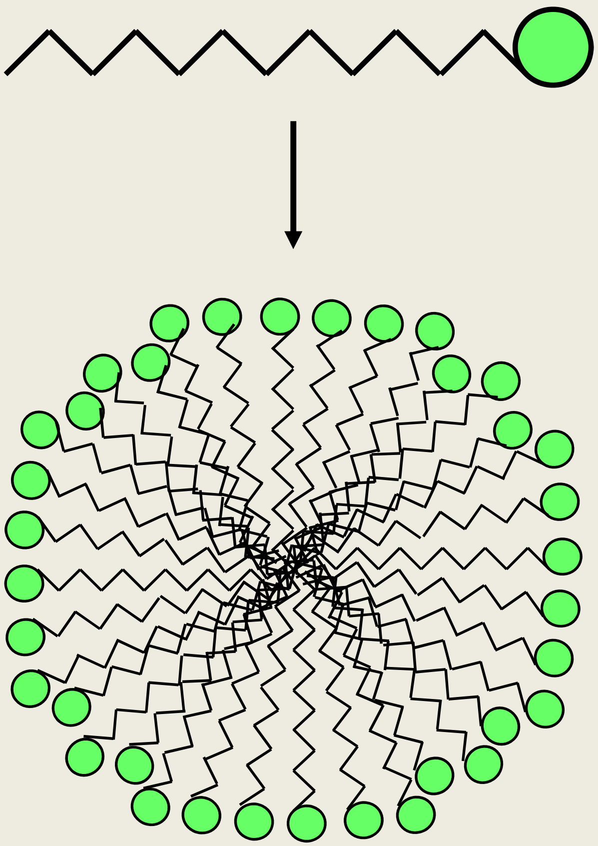
; Dendrimers have large cavities.

→ possible to contain a lot of guest molecules

→ release guest molecules size selectively upon hydrolysis of the dense outer shell

3.3 Dendritic Micelles

Surfactant

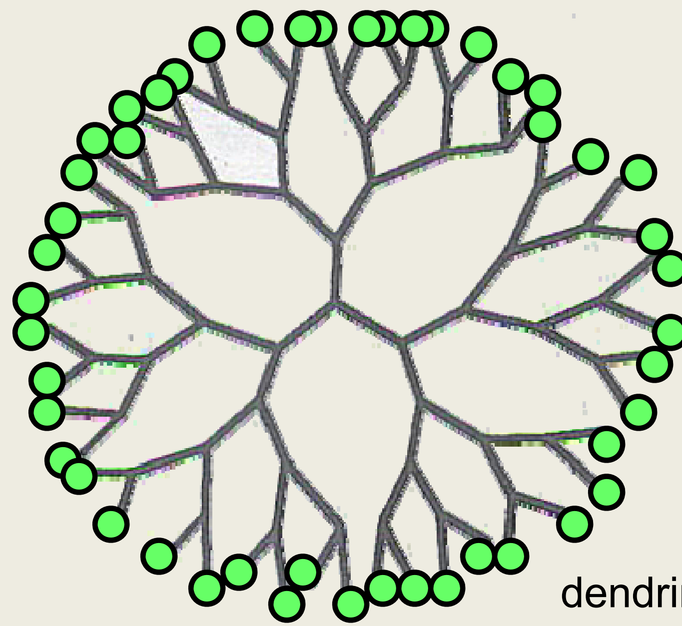


Micelle

; The molecular structure of dendrimer are similar to micelle formed by surfactant.

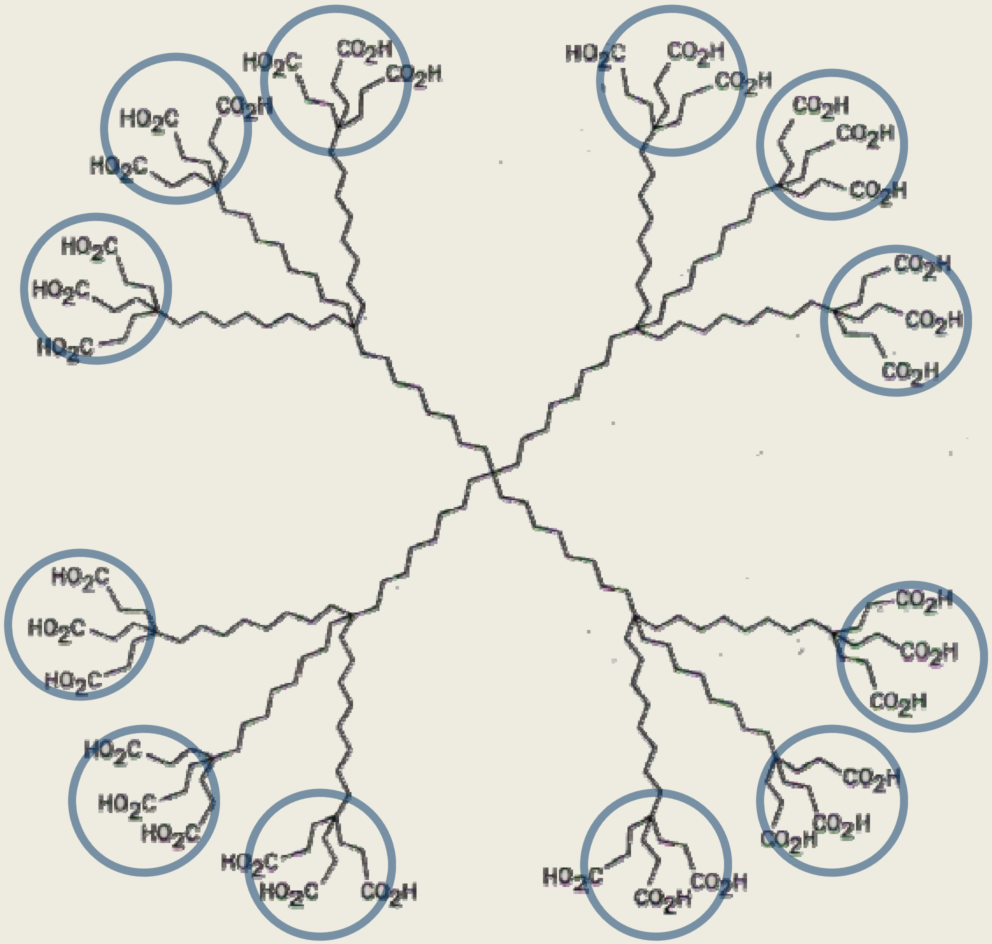
; Dendrimers can be a “unimolecular micelle”
→ Not to require micellization condition

≒



dendrimer

3. The Ideas for Finding Applications of Dendrimers



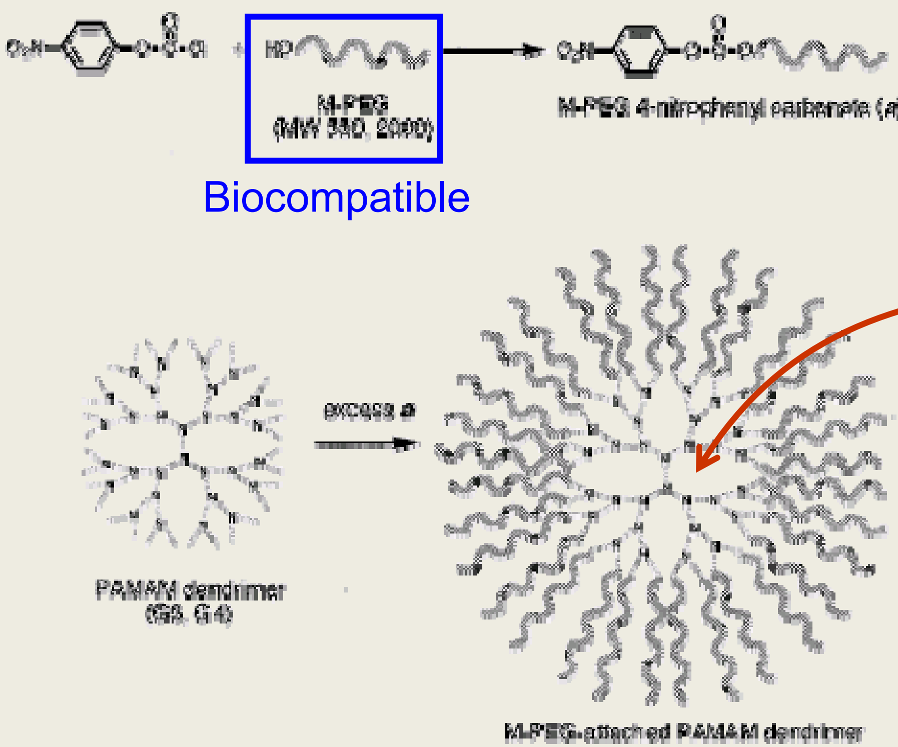
; braching unit – aliphatic chain (hydrophobic)

terminal groups – carboxylic acid (hydrophilic)

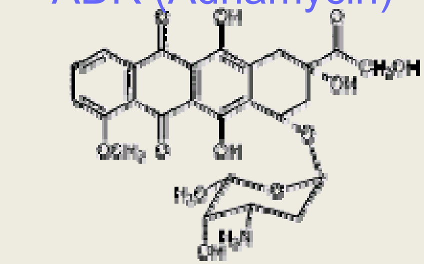
→ “unimolecular micelles”

3.4 Dendrimers in Drug Delivery Systems

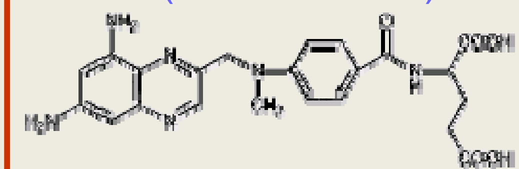
; The studies on DDS by using dendrimers are based on host-guest chemistry and dendritic micelle concept.



(A) ADR (Adriamycin)



(B) MTX (Methotrexate)



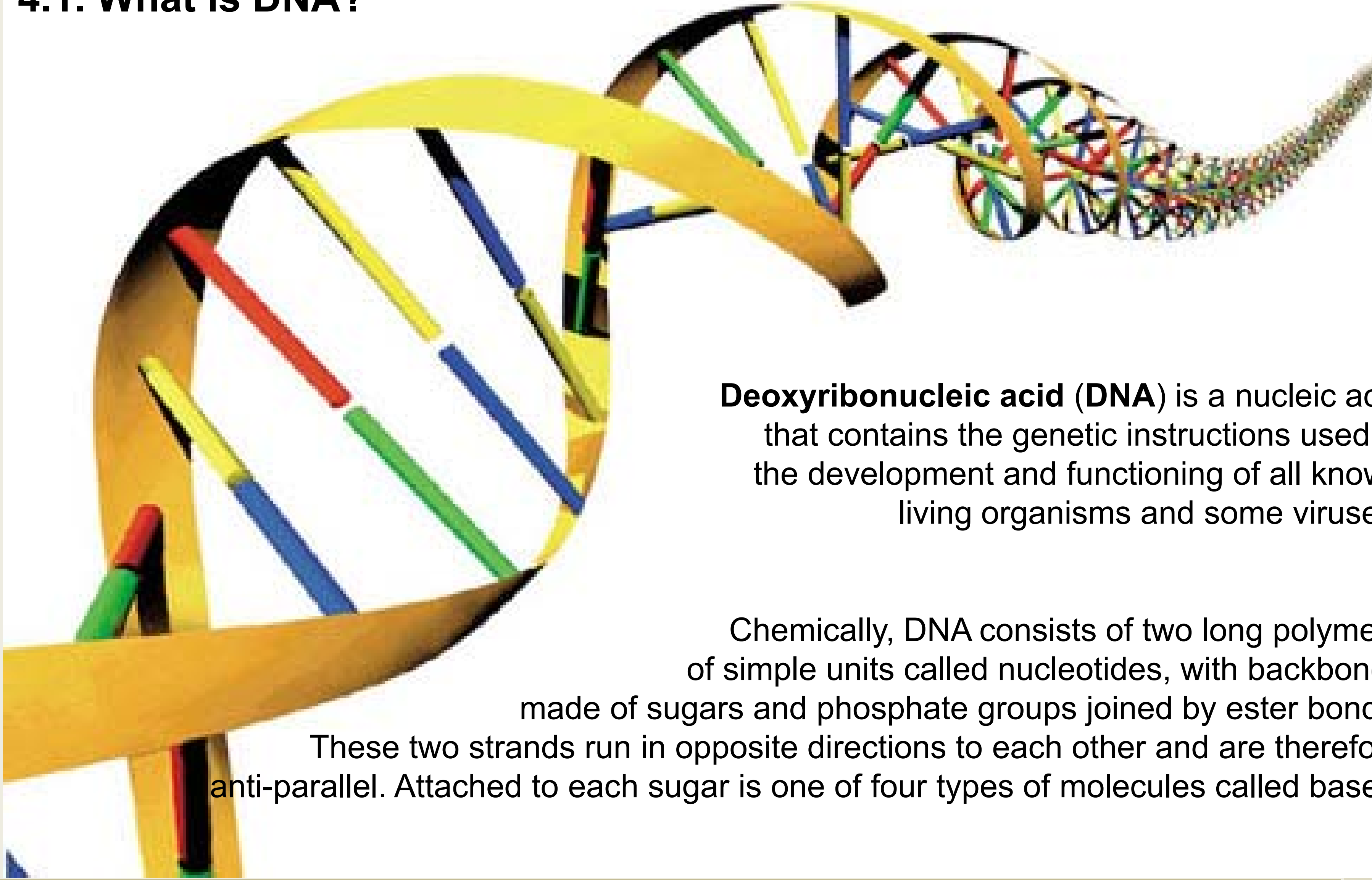
Anticancer drugs

→ These Dendrimers having an interior for encapsulation of drugs and a biocompatible surface

Ref. Kojima et al. *Bioconjugate Chem*, **11** (2000) 910

4. Introduction of DNA

4.1. What is DNA?

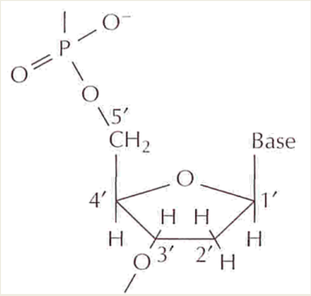


Deoxyribonucleic acid (**DNA**) is a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms and some viruses.

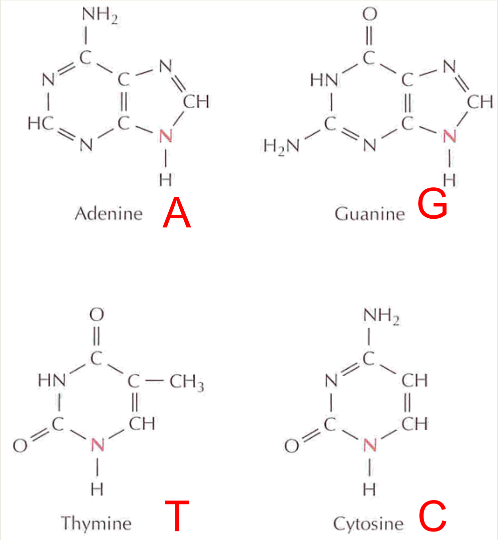
Chemically, DNA consists of two long polymers of simple units called nucleotides, with backbones made of sugars and phosphate groups joined by ester bonds. These two strands run in opposite directions to each other and are therefore anti-parallel. Attached to each sugar is one of four types of molecules called bases.

4.2. Structure of DNA

- Nucleotide (deoxyribonucleotide)
  - the basic unit of a DNA strand
  - A deoxyribonucleotide has three components: a pentose sugar or deoxyribose, a phospate group, and one of four nitrogen-containing bases.
  - An organic base attached to the 1' carbon of the doxyribose sugar of the n ucleotide.
  - A phosphate group attached to the 5' carbon of the sugar moiety.

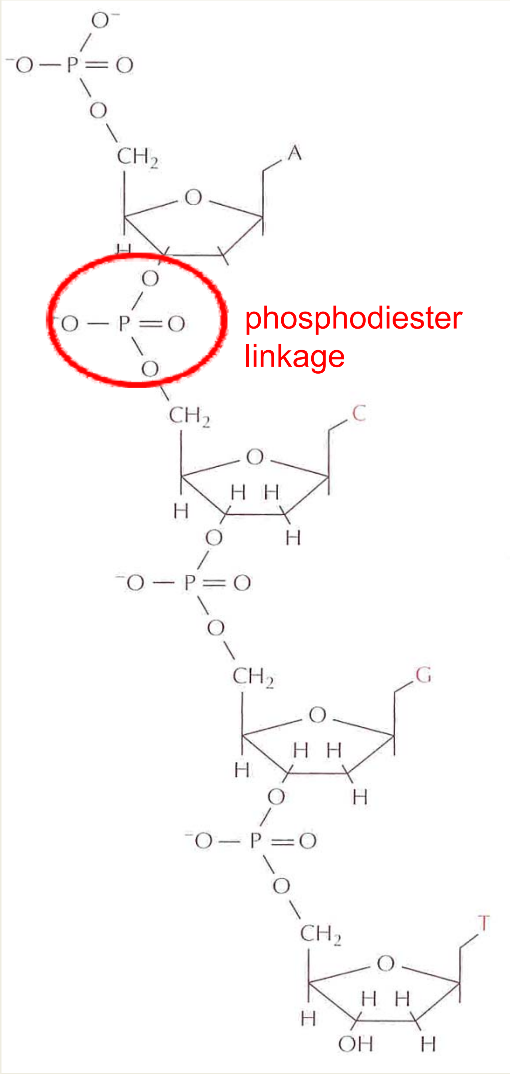


Nucleotide



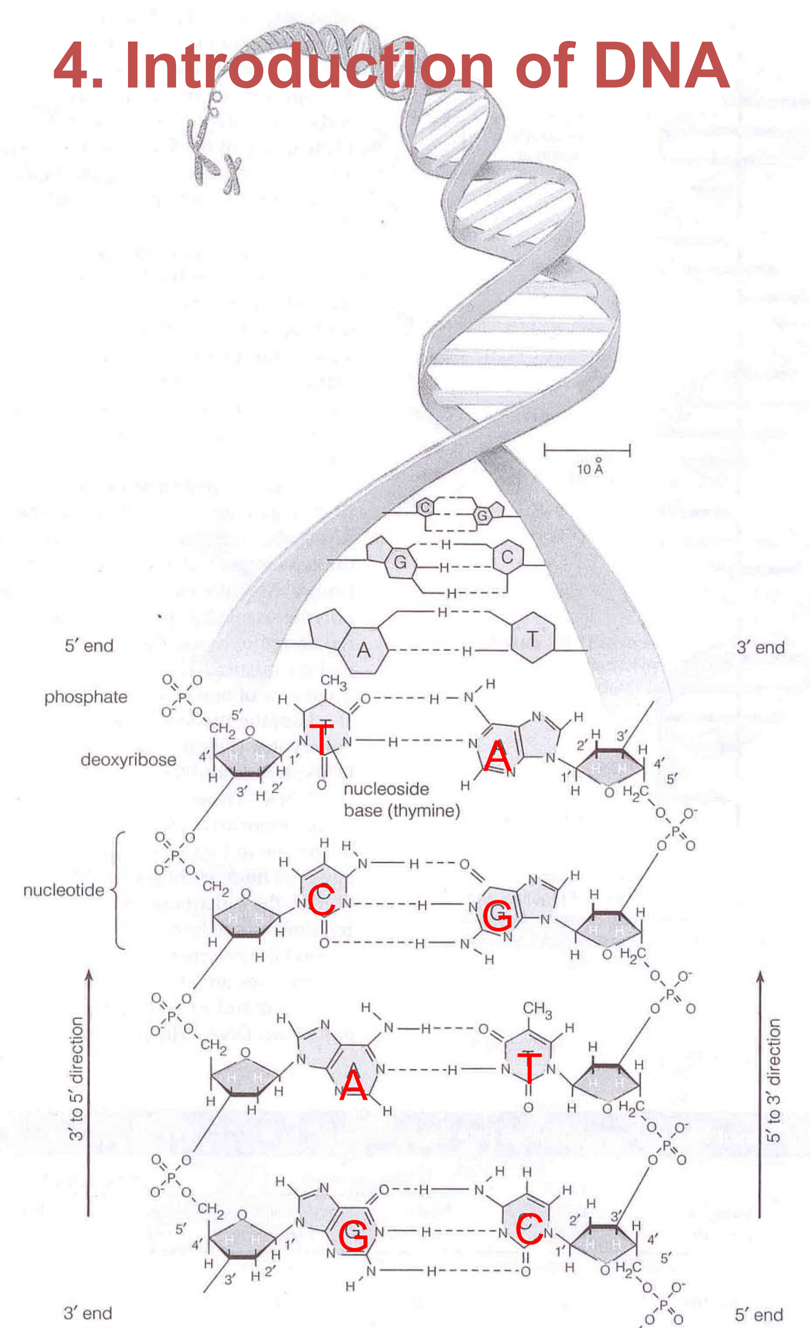
Four bases of a DNA molecules

4.2. Structure of DNA

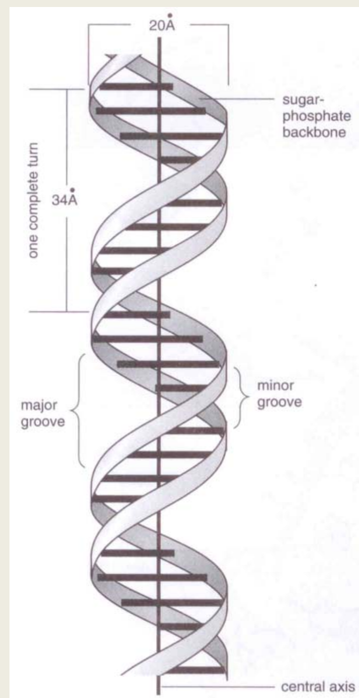


- DNA (Deoxyribonucleic acid)
  - a long polymer consisting of repeating units called deoxyribonucleotides
  - The nucleotide of a DNA chain are linked by phosphodiester bonds between the 5'-phosphate group of one nucleotide and the 3'-hydroxyl group of another nucleotide.
  - A DNA strand may be made up of many thousands of nucleotides.

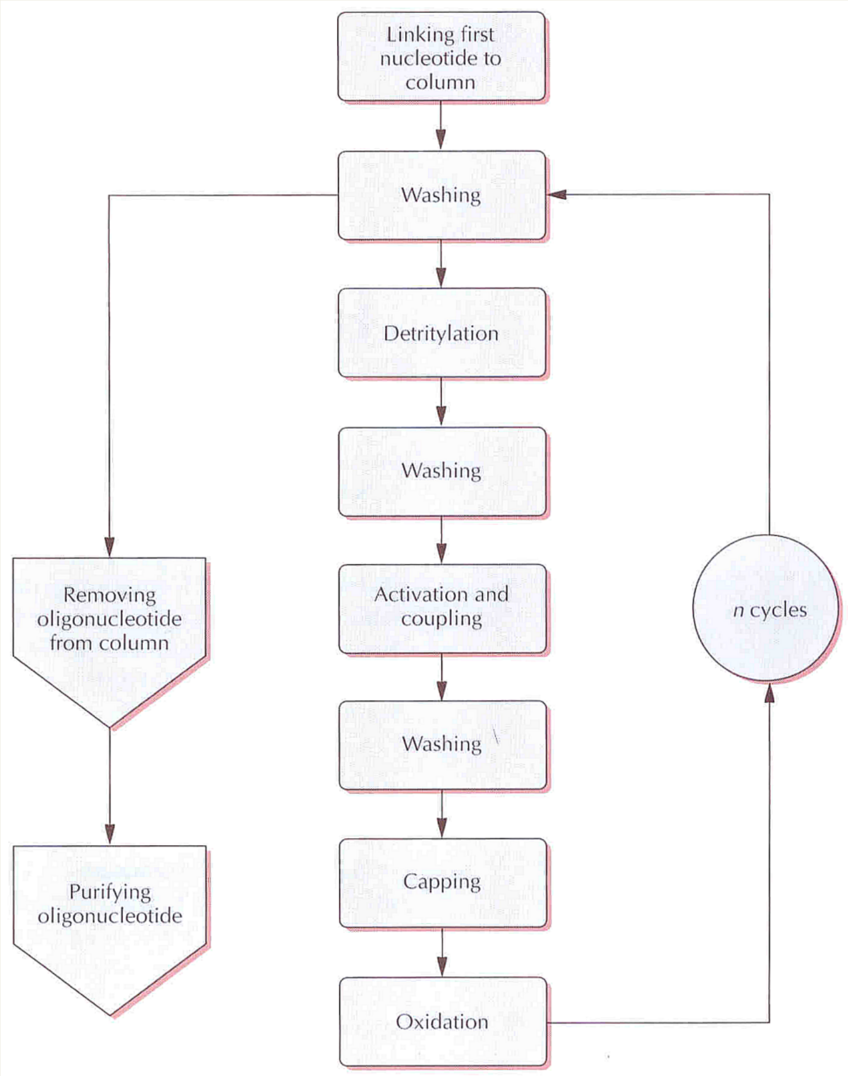
4. Introduction of DNA



- Double-stranded molecule (Double helix)
  - Hydrogen bonding between opposite bases holds the two strands of the DNA molecule together. (A↔T, G ↔ C)
  - For hydrogen bonding of the bases, the strands must be antiparallel to one another so that one strand goes from 5‘ to 3‘ and the other 3‘ to 5‘.
  - The two strands do not spontaneously separate under physiological conditions because the many hydrogen bonds keep the base pairs together.



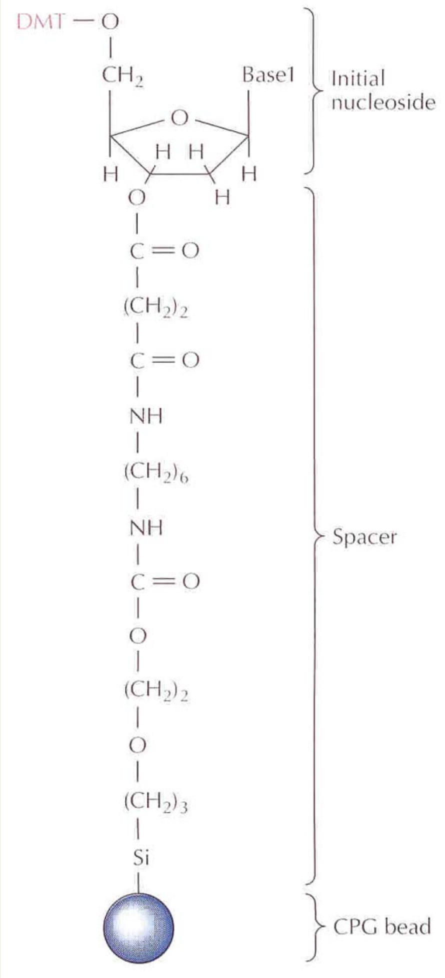
4.3. Chemical synthesis of DNA



Flow chart for phosphoramidite method

- Phosphoramidite method
  - Chemical synthesis of DNA oligonucleotides
  - Solid-phase synthesis; attachment of the growing group DNA strand to a solid support
  - The multistep synthesis can be conducted in one reaction vessel.

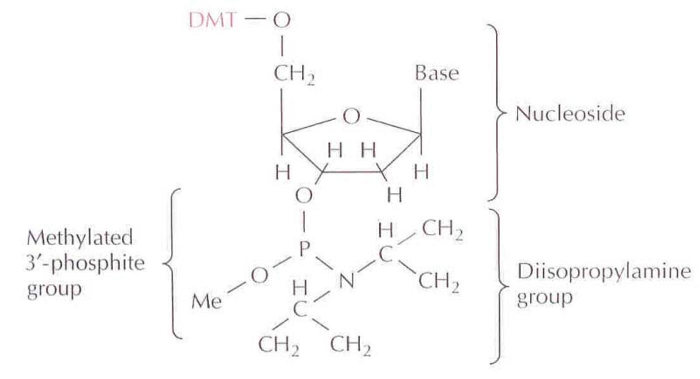
4. Introduction of DNA



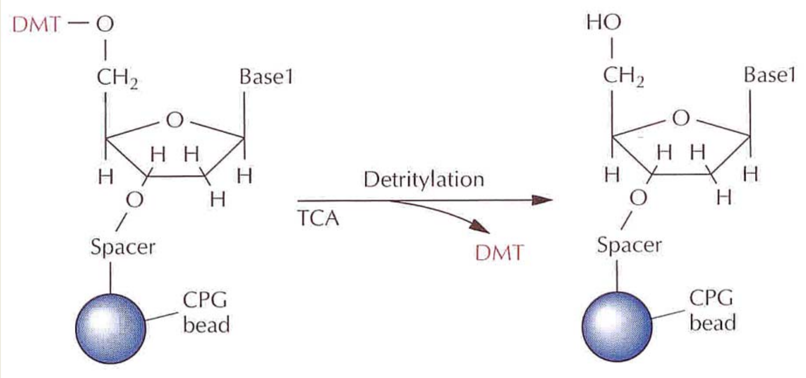
- Linking first nucleotide to column (1st step)
  - The initial nucleoside is attached to an inert solid support(controlled pore glass, CPG).
  - A dimethoxytrityl(DMT) group has been attached to the 5'-terminus of of the initial nucleoside to prevent 5'-hydroxyl group from reacting nonspecifically, prior to the addition of the second nucleotide.

※ Phosphoramidite

- A methyl groups protects the 3'-phosphite, and DMT group is on 5'-hydroxyl group of the deoxyribose sugar.



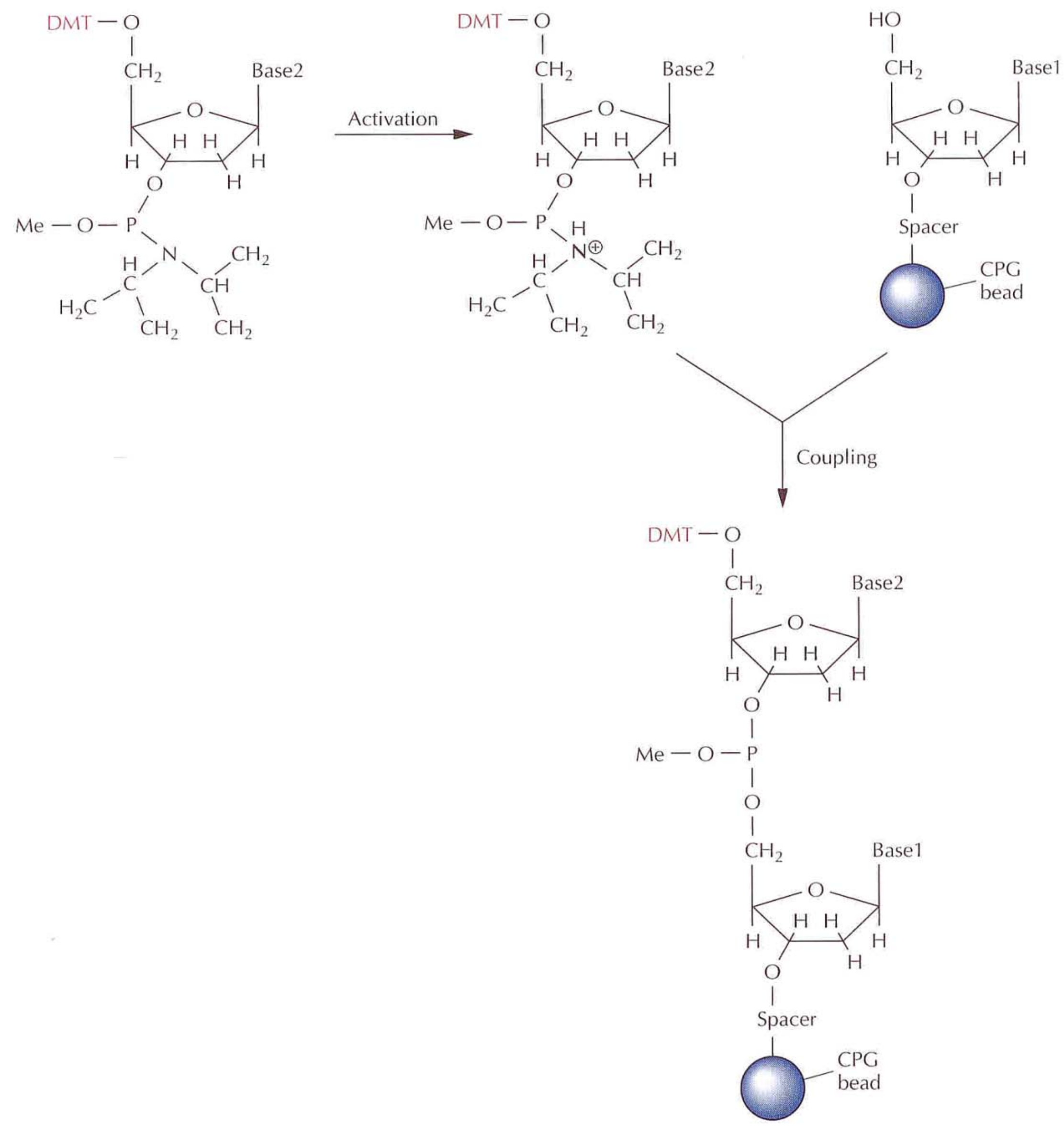
4. Introduction of DNA



- Washing (After all steps)
  - Washing with anhydrous reagent to remove water and any nucleophiles
  - Flushing with Ar to purge anhydrous reagent

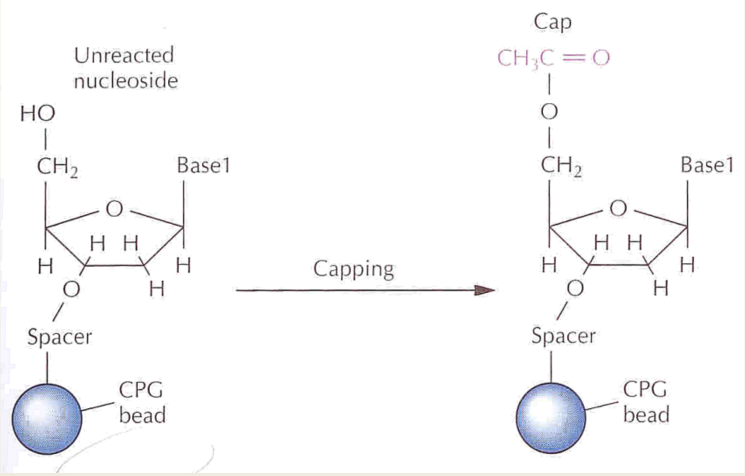
- Detritylation (2nd step)
  - 5'-DMT group is removed from the attached nucleoside by treatment with trichloroacetic acid(TCA) to yield a reactive 5'-hydroxyl group

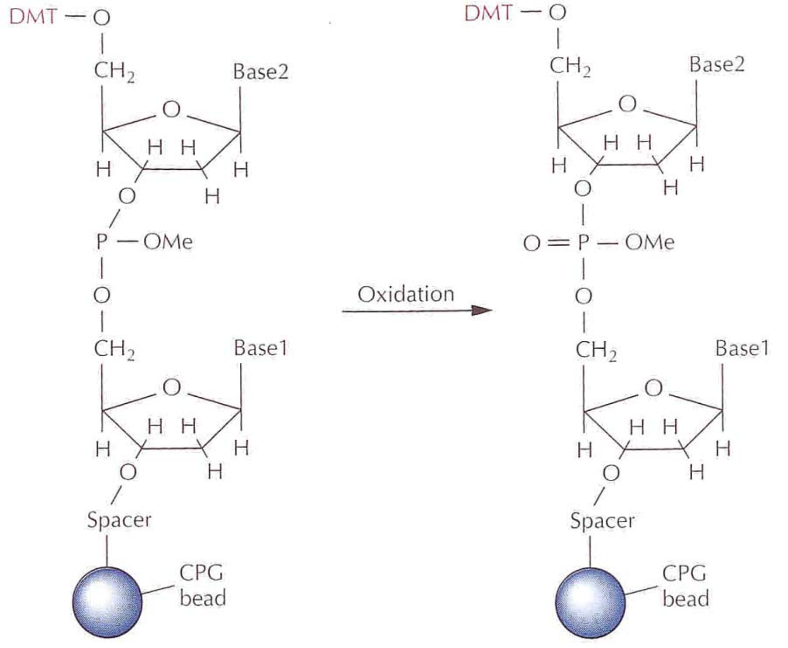
4. Introduction of DNA



- Activation and Coupling (3^{rd} step)
  - Addition of tetrazole: activation of a phosphoramidite
  - 3'-phosphite forms covalent bond with the 5'-hydroxyl group of initial nucleoside.

4. Introduction of DNA



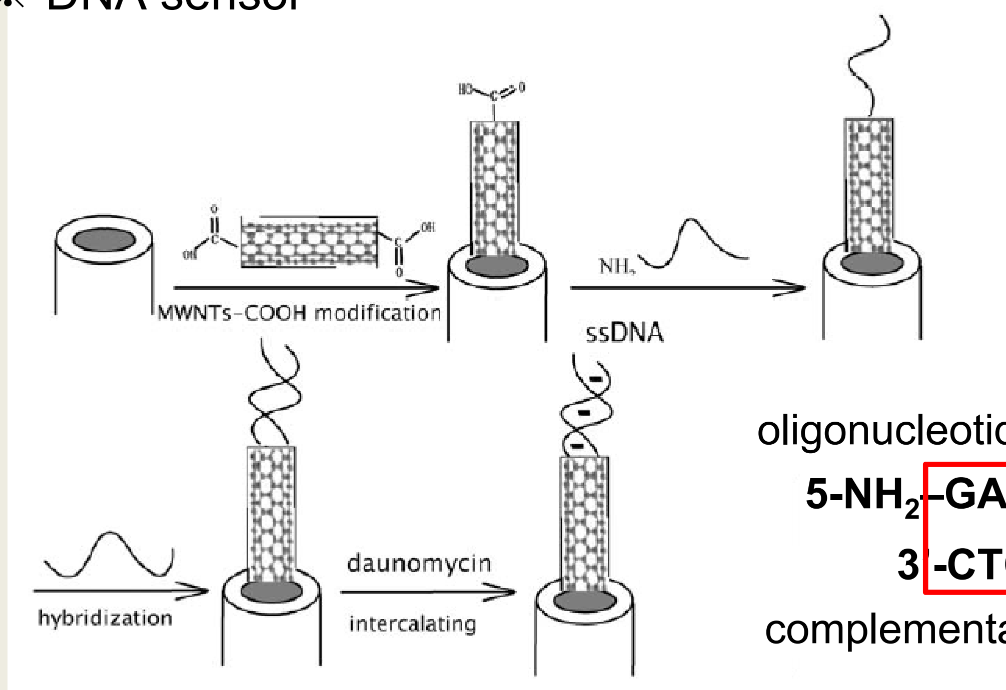


- Capping (4th step)
  - The unlinked residues must be prevented form linking to the next nucleotide during the following cycle.
  - Acetylation of the unreacted 5'-hydroxylg groups.
- Oxidation (5th step)
  - The internucleotide linkage is in the form of a phosphite triester bond, which is unstable and prone to breakage in presence of either acid or base.
  - The phosphite triester is oxidized with an iodine mixture to form the more stable pentavalent phosphate triester.

4.4. DNA hybridization

- DNA hybridization
  - The pairing of two DNA molecules often from different sources
  - Driving force: hydrogen bonding between nucleotides.

※ DNA sensor



DNA hybridization
(Hydrogen bonding: A↔T, G ↔ C)

oligonucleotide probe

5-NH_2–GAGCGGCGCAACATTTCAGGTCGA-3'

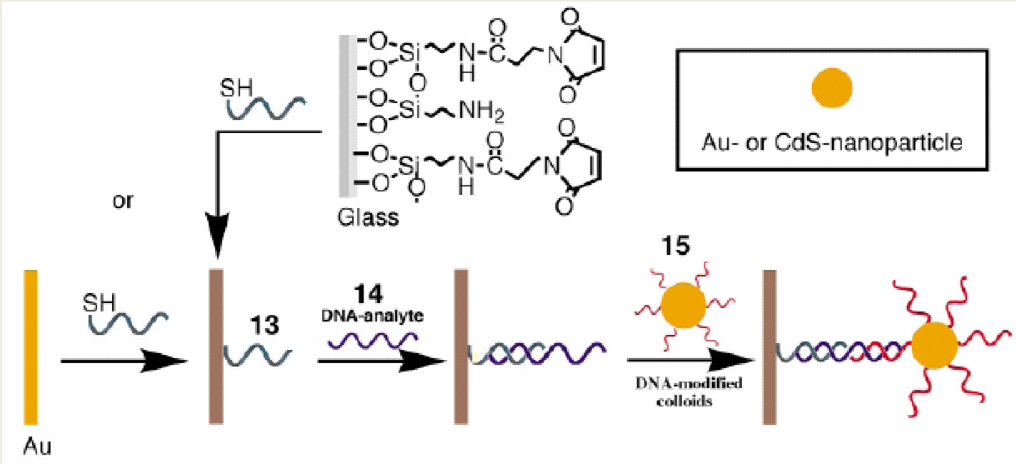
3'-CTCGCCGCGTTGTAAAGTCCAGCT-5'

complementary target oligonucleotides

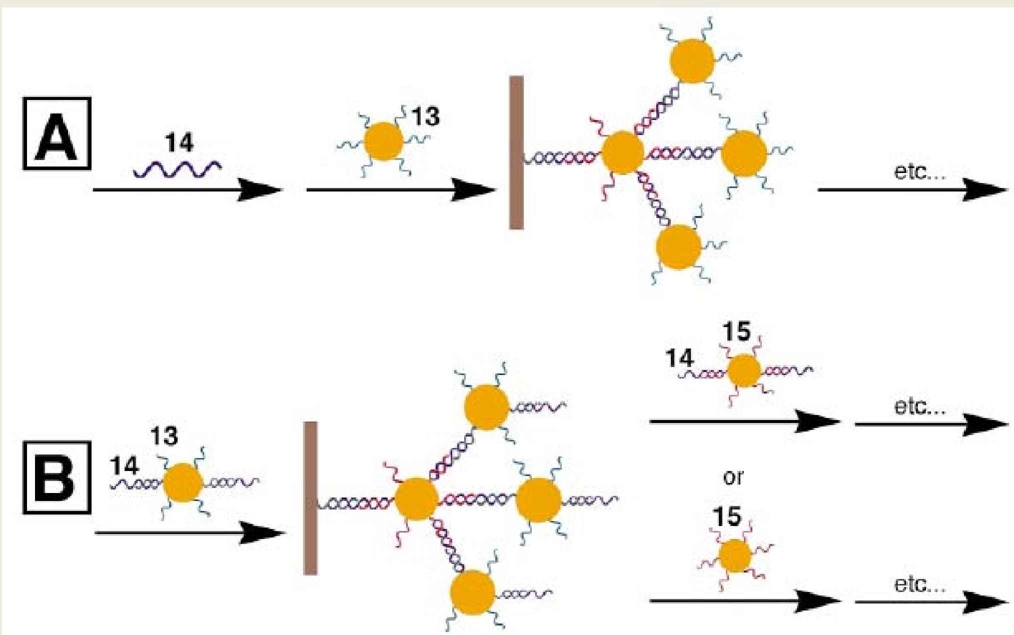
***Anal. Bioanal. Chem.* 2003, 375, 287-293**

4. Introduction of DNA

※ DNA-linked nanoparticle superstructure



- DNA is a promising construction material for artificial nano-structured devices.
- One of attractive features of DN A is the great meachnical rigidit y of short double helices, so that they behave effectively like a rigid rod spacer.



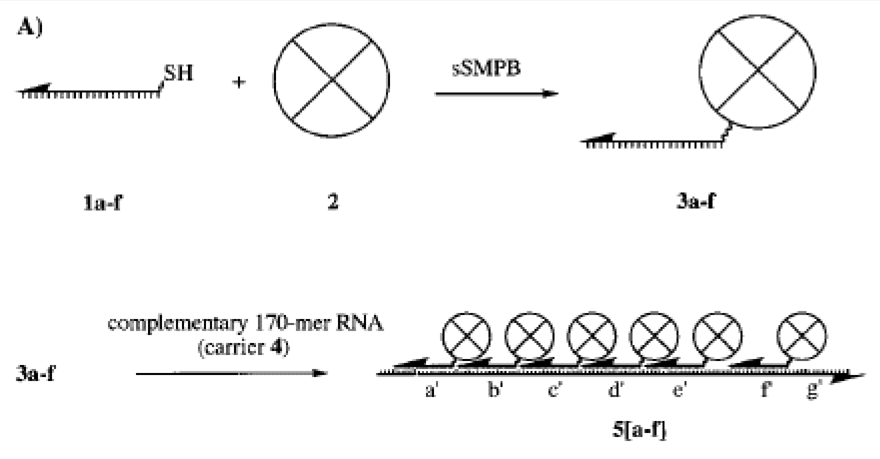
Example oligonucleotides:

13 = 5'-TCTATCCTACGCT-$(CH_2)_6$-SH-3'
14 = 5'-AGCGTAGGATAGATATACGGTTCGCGC-3'
15 = 5'-HS-$(CH_2)_6$-GCGCGAACCGTATA-3'

***Chem. Commun.* 2001, 2035-2045**

5.1. DNA-directed assembly of proteins

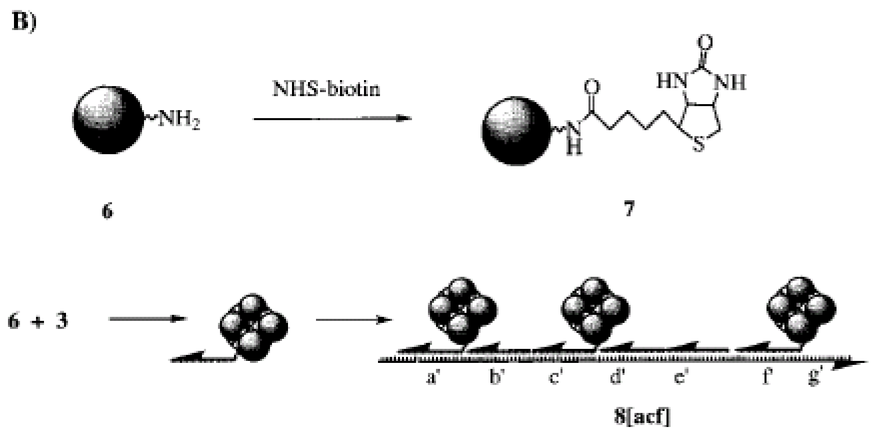
- Covalent DNA-Streptavidin(STV) Conjugates
  - STV's native binding capacity for four biotin molecules is supplemented by a highly specific binding site for complementary nucleic acids.
  - The conjugates can be utilized as biomolecular adapters for positioning biotinylated components along a nucleic acid backbone.

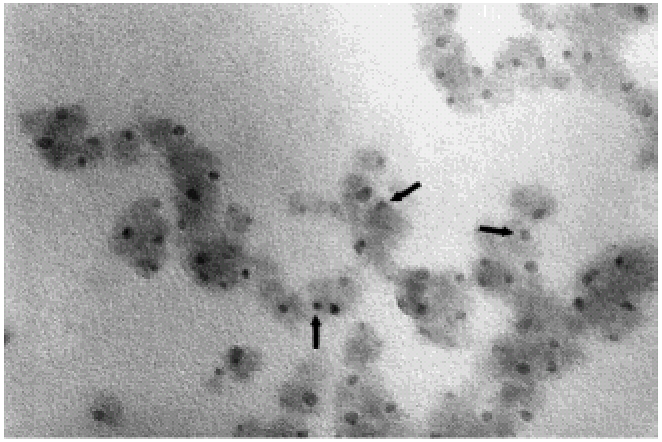


1: 5'-thiol-modified oligonucleotides
2: streptavidin(STV)
3: DNA-STV conjugates
4: RNA(5'-a'-b'-c'-d'-e'-f'-g'-3')
5: supramolecular aggregates

Angew. Chem. Int. Ed. **1998, 37, 2265-2268**

5. Self-assembled nanostrucutres based on DNA





8

6: Monoamino-modified gold cluster

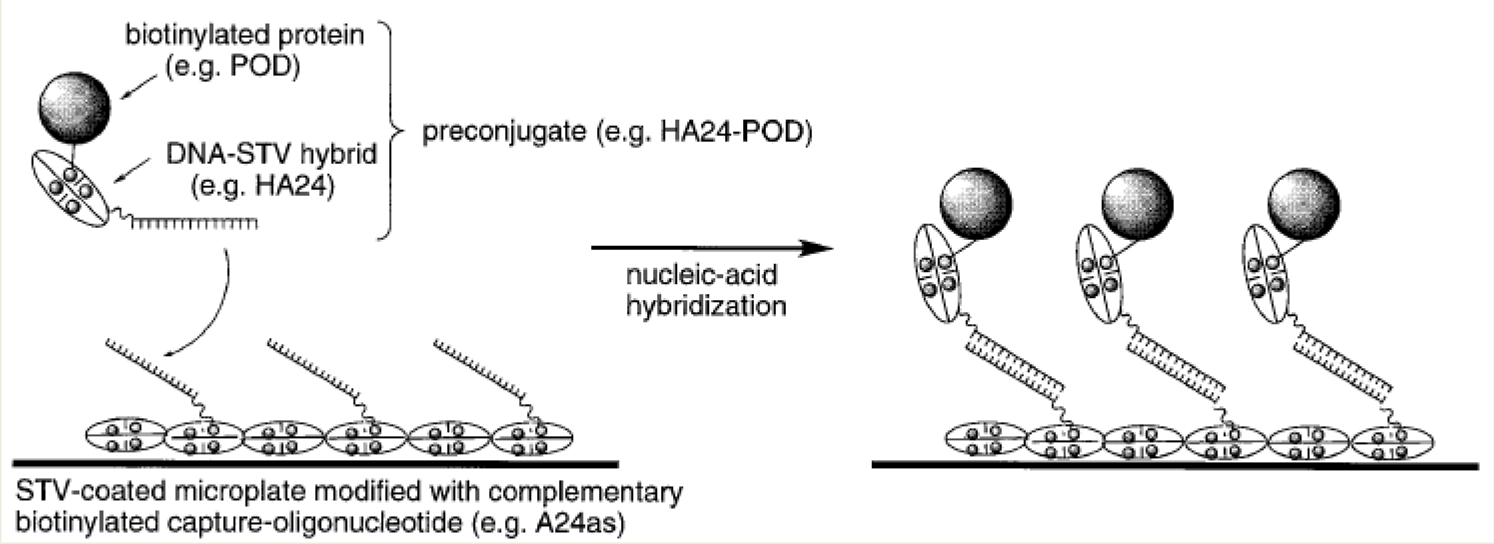
7: biotinylated cluster

8: supramolecular aggregates

Angew. Chem. Int. Ed. 1998, 37, 2265-2268

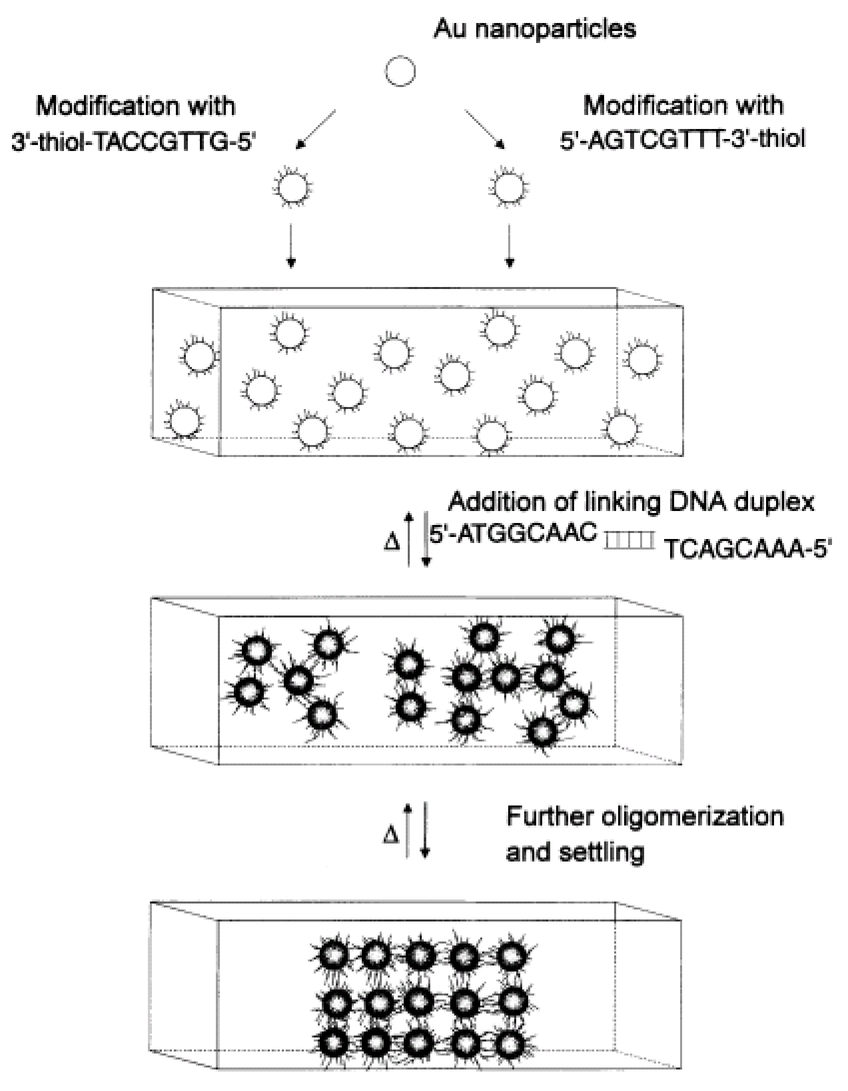
5. Self-assembled nanostrucutres based on DNA

- DNA-Directed Immobilization
  - The noncovalent attachment of oligonucleotide fragments to various biotinylated biomaterials
  - The single-stranded DNA-tagged proteins were immobilized to compliemtary surface-bound capture oligonucleotides by means of specific nucleic acid hybridization.



Anal. Biochem. **1999, 268, 54-63**

5.2. Organization of inorganic nanoclusters

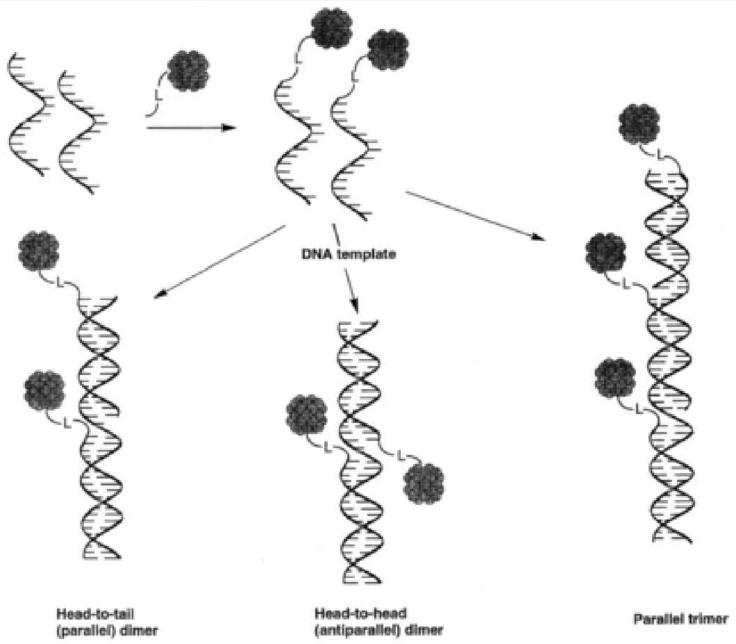


- A DNA-based method for assembling nanoparticles into macroscopic materials
  - Many methods have been developed for assembling colloidal particles into useful aggregates and materials.
  - Colloidal Au nanoparticles are reversibly assembled into macroscopic aggregates through a DNA-based method.
  - This assembly process can be reversed by thermal denaturation.

Nature. 1996, 382, 607-609

5. Self-assembled nanostrucutres based on DNA

- Organization of Nanocrystal molecules using DNA
  - Au nanocrystals are organized into spatially defined structures based on DNA hybridization.
  - Individual Au nanocrystals are attached to single stranded DNA oligonucleotides of difined length and sequence.
  - DNA-nanocrystal conjugates assemble into dimers and trimers on addition of complementary single-stranded DNA template.

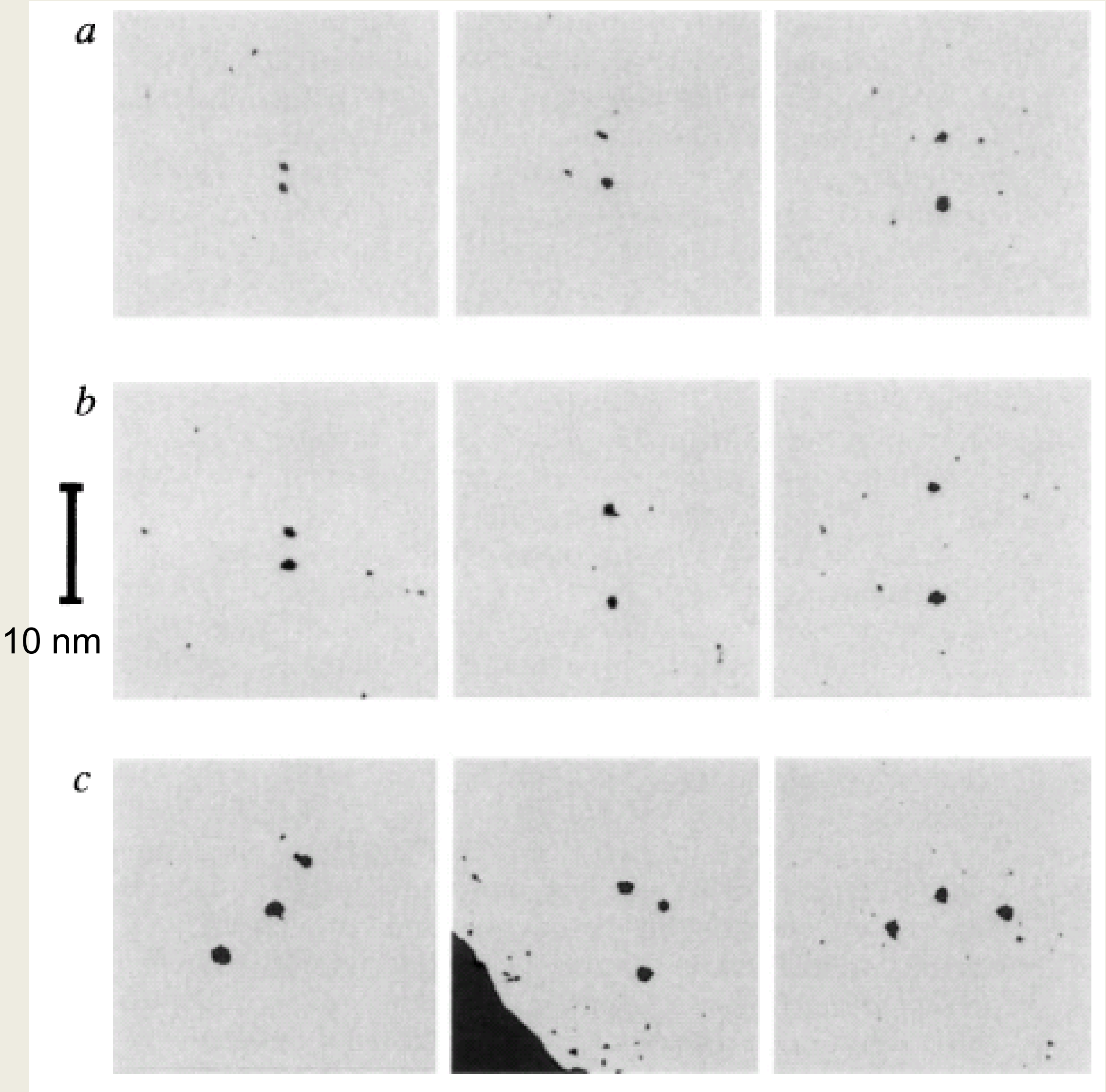


oligo**1**) 5'-HS-CAGTCAGGCAGTCAGTCA-3'
oligo**3**) 5'-HS-CTTGCACTAGTCCTTGAG-3'
oligo**4**) 5'-CAGTCAGGCAGTCAGTCA-SH-3‘

template**2**) 5'-TGACTGACTGCCTGACTGTTGACTGACTGC CTGACTG-3'
template**5**) 5'-CTCAAGGACTAGTGCAAGTTGACTGACTGC CTGACTG-3'
template**6**) 5'-TGACTGACTGCCTGACTGTTGACTGACTGC CTGACTGTTGACTGACTGCCTGACTG-3'

Nature. **1996, 382, 609-611**

5. Self-assembled nanostrucutres based on DNA



Head-to-head

oligo1 + template2

Head-to-tail

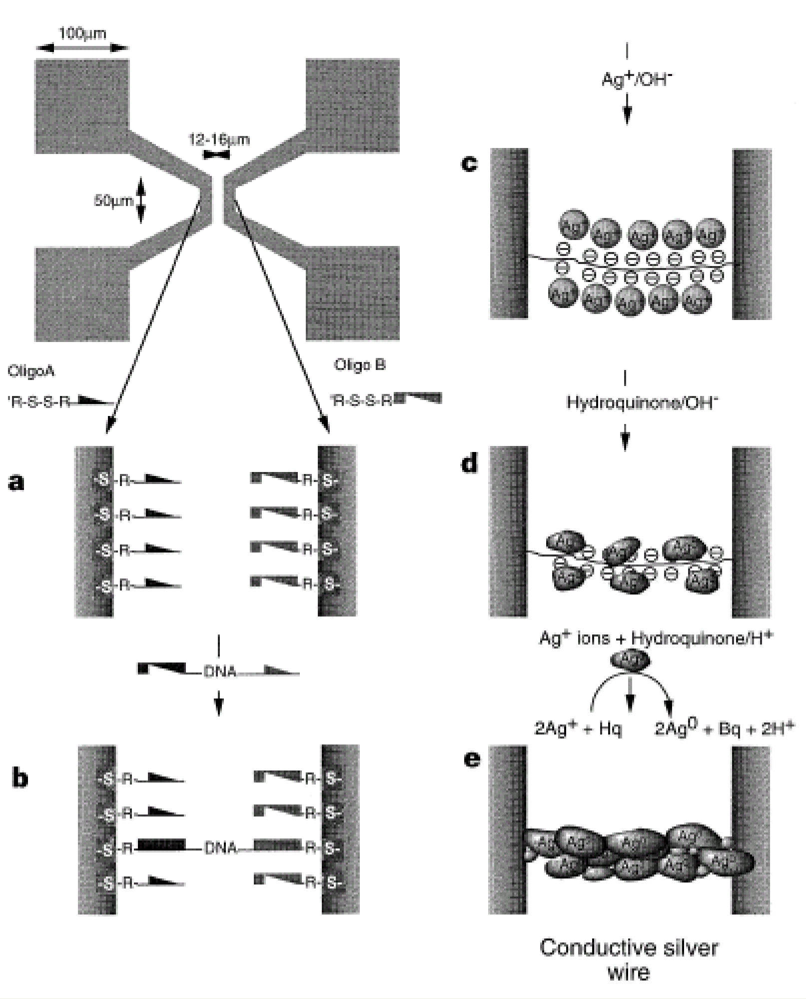
oligo3 + oligo4 + template 5

Trimer

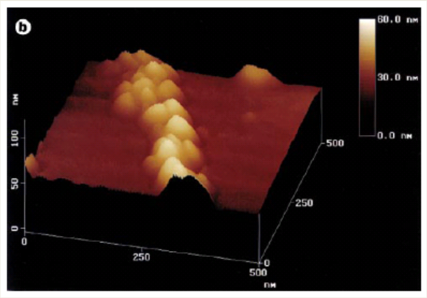
oligo1 + template6

Nature. 1996, 382, 609-611

5.3. DNA-templated synthesis



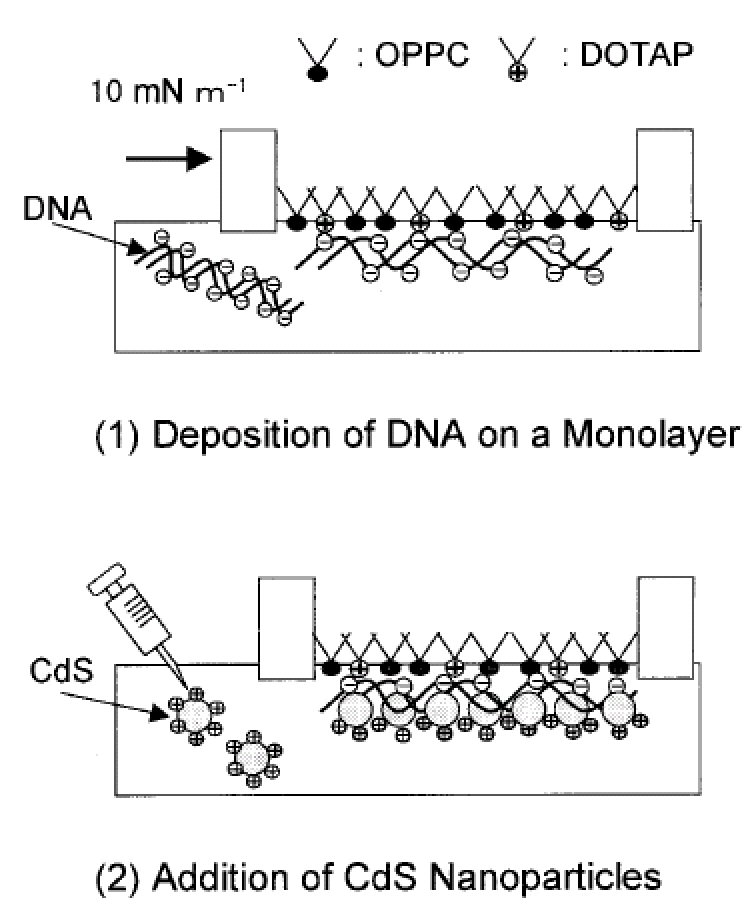
- The electrostatic and topographic properties of the DNA molecule is utilized as template to synthesize nanostructures.
- Silver metals is vctorially deposited along the DNA molecule(phosphate backbone).
- Three-step chemical deposition:
  1. selective localization of silver ion (Ag^+/Na^+ ion exchange)
  2. formation of complexes between the silver and the DNA molecules
  3. reduction of silver ion-exchanged DNA



12 μm long, 100 nm wide conductive silver wire

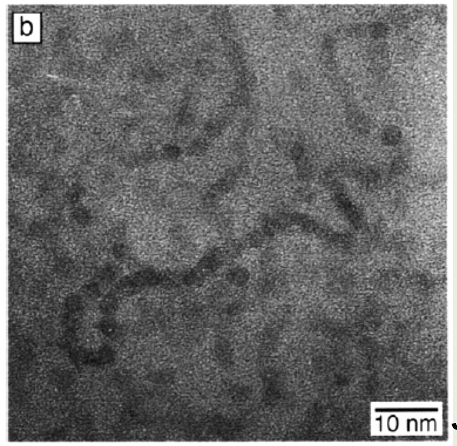
Nature. 1998, 391, 775-778

5. Self-assembled nanostrucutres based on DNA



※ dioleoyl trimethylammonium propane (DOTAP)
β-oleoyl-γ-palmitoyl L-α-phosphatidylcholine (OPPC)

- Preformed, positively charged 3 nm CdS nanoparticles are deposited on DNA template.
- The particles are arranged in a dense quasi-one-dimensional packing.
- Using the electrostatic interaction between the cationic surface modifiers on the CdS nanoparticles and the phosphate groups in DNA double strands as a template.



J. Phys. Chem. B **1999, 103, 8799-8803**