Title	Far-from-equilibrium behavior of ten-micrometer-scale artificial chemical assemblies : Autocatalytic vesicular self-reproduction and light-powered crystalline self-oscillation
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Far-from-equilibrium behavior of ten-micrometer-scale artificial chemical assemblies

— Autocatalytic vesicular self-reproduction and light-powered crystalline self-oscillation

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July 10-11, 2023. Systems Chemistry Virtual Symposium 2023
The presentation slides are available from HUSCAP
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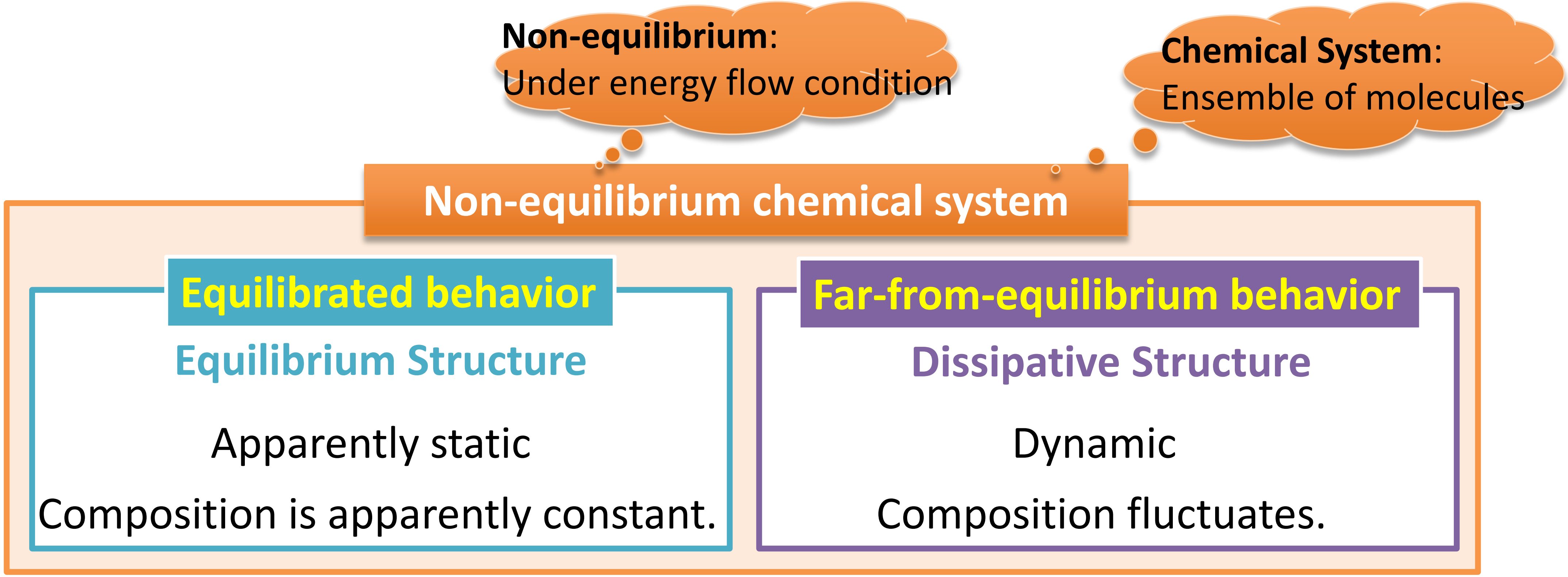
What is “far-from-equilibrium” in chemical thermodynamics

Far-from-equilibrium system is a chemical system with fluctuation in composition.



Non-equilibrium:
Under energy flow condition

Chemical System:
Ensemble of molecules

Non-equilibrium chemical system

Equilibrated behavior

Equilibrium Structure

Apparently static

Composition is apparently constant.

Far-from-equilibrium behavior

Dissipative Structure

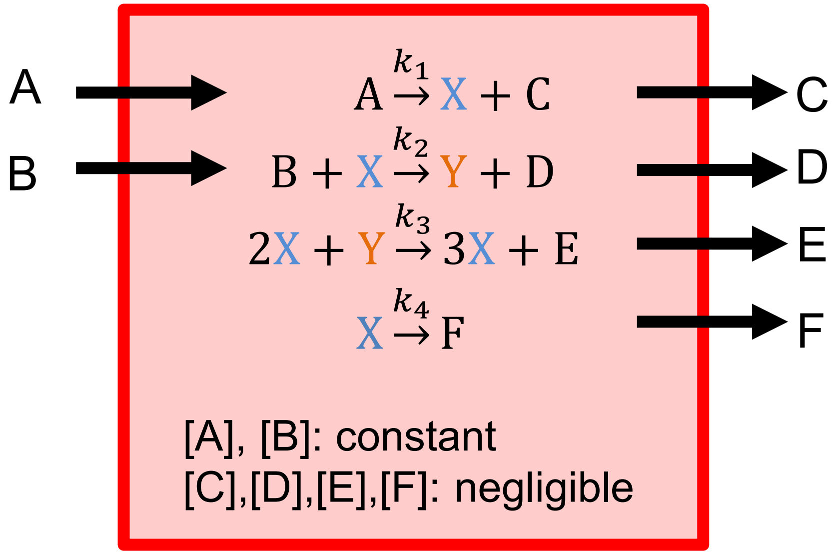
Dynamic

Composition fluctuates.

The feature of far-from-equilibrium
is very different from equilibrium.

Brusselator, a model reaction system for chemical oscillation

Concept of Brusselator: a model for BZ-reaction



$$\mathrm{A} \xrightarrow{k_1} \mathrm{X} + \mathrm{C}$$
$$\mathrm{B} + \mathrm{X} \xrightarrow{k_2} \mathrm{Y} + \mathrm{D}$$
$$2\mathrm{X} + \mathrm{Y} \xrightarrow{k_3} 3\mathrm{X} + \mathrm{E}$$
$$\mathrm{X} \xrightarrow{k_4} \mathrm{F}$$

[A], [B]: constant
[C],[D],[E],[F]: negligible

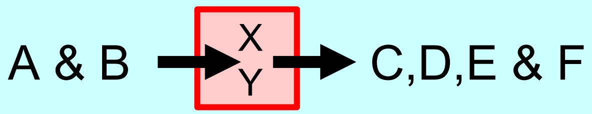
X and Y cannot pass through the wall.

The 3rd step:
autocatalytic process
where X promotes the decrease of Y.
The 2nd step:
X causes the increase of Y.

If you cannot image the condition shown left……

A huge vessel

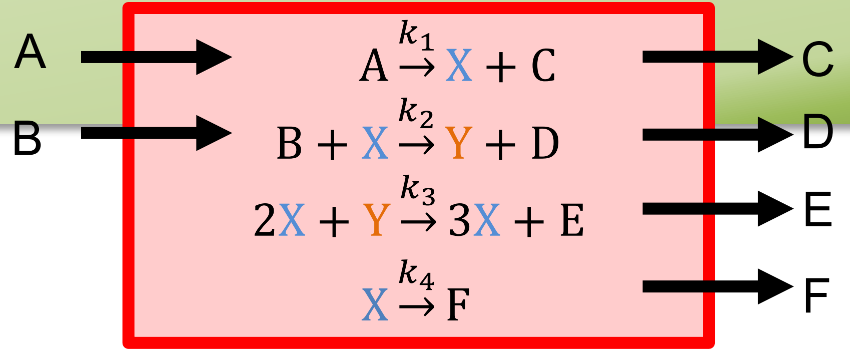
Objective system



X and Y cannot pass through the wall.

[A], [B] are apparently constant.
[C],[D],[E],[F] are apparently zero.

What is “far-from-equilibrium”

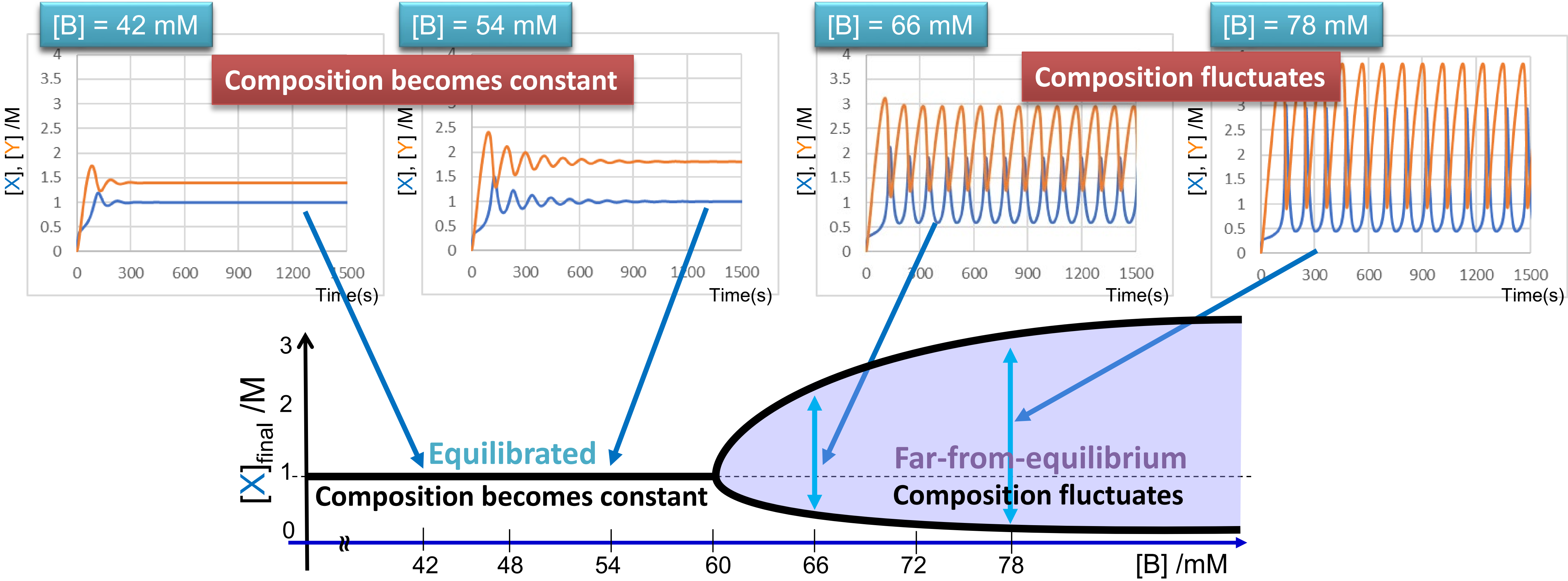


$$A \xrightarrow{k_1} X + C$$
$$B + X \xrightarrow{k_2} Y + D$$
$$2X + Y \xrightarrow{k_3} 3X + E$$
$$X \xrightarrow{k_4} F$$

k_1 = 1.0 /s
k_2 = 2.0 /M s
k_3 = 0.06 /M^2 s
k_4 = 0.06 /s
[A] = 60 mM
[B] : variable

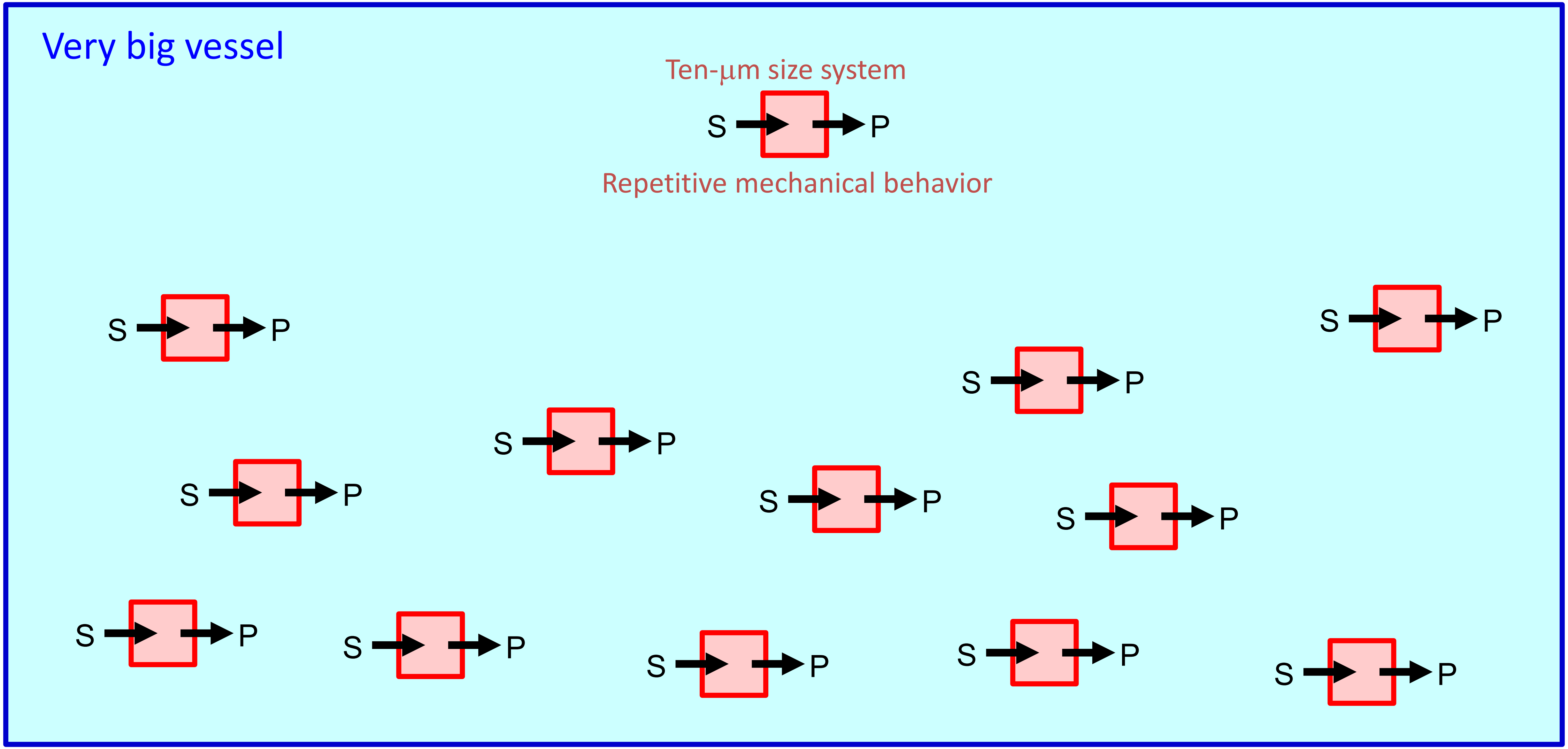
Concept of Brusselator: a model for BZ-reaction

All of them are open systems with flow of substrates.



Ilya Prigogine found both **Equilibrium Structure** and **Dissipative Structure** in a chemical system with energy flow.
In the above example, **[B] characterizes the behavior of the system**.

My research results



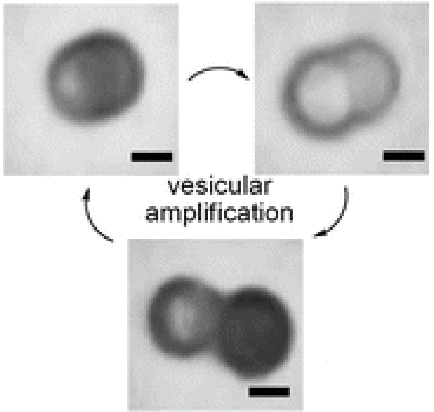
Very big vessel

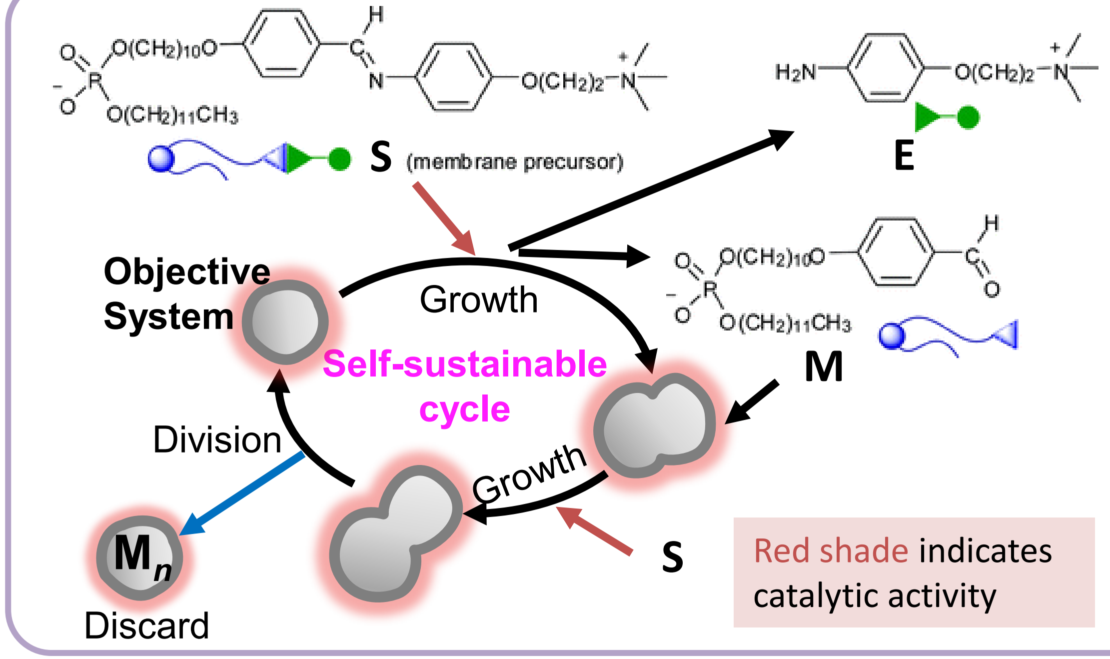
Ten-μm size system

Repetitive mechanical behavior

Self-continuous vesicular growth and division: Autocatalytic vesicle reproduction

Takahashi, Sugawara, et al
***Chem. Commun.* 46, 8791-8793 (2010).**
Other groups:
N. Devaraj, *PNAS* (2015);
P. Luisi, *JACS* (1994).



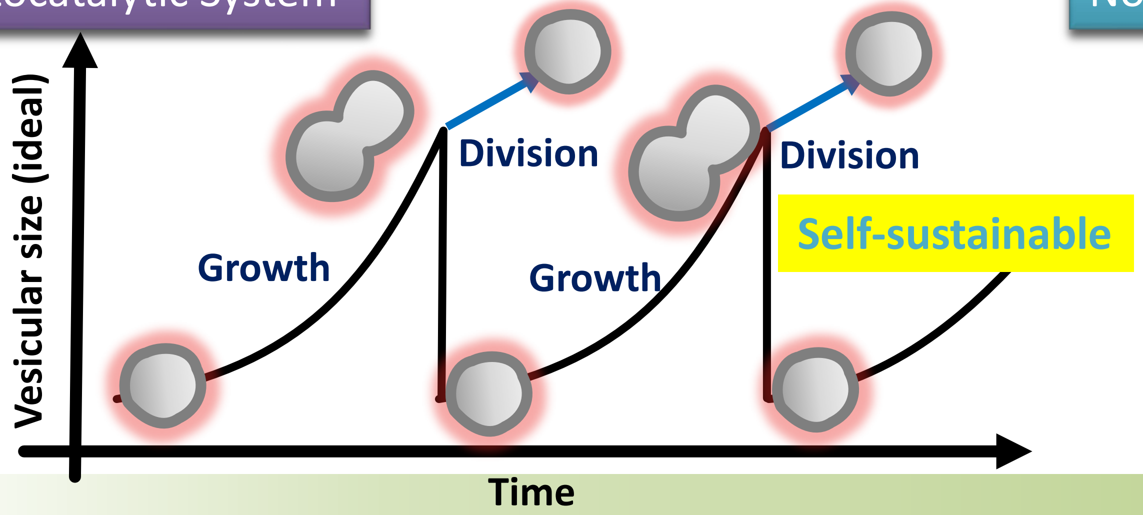


Red shade indicates catalytic activity

- Local proton activity surrounding anionic vesicle catalyze the hydrolysis of **S** to form **M**.
- **M** becomes a component of vesicle.

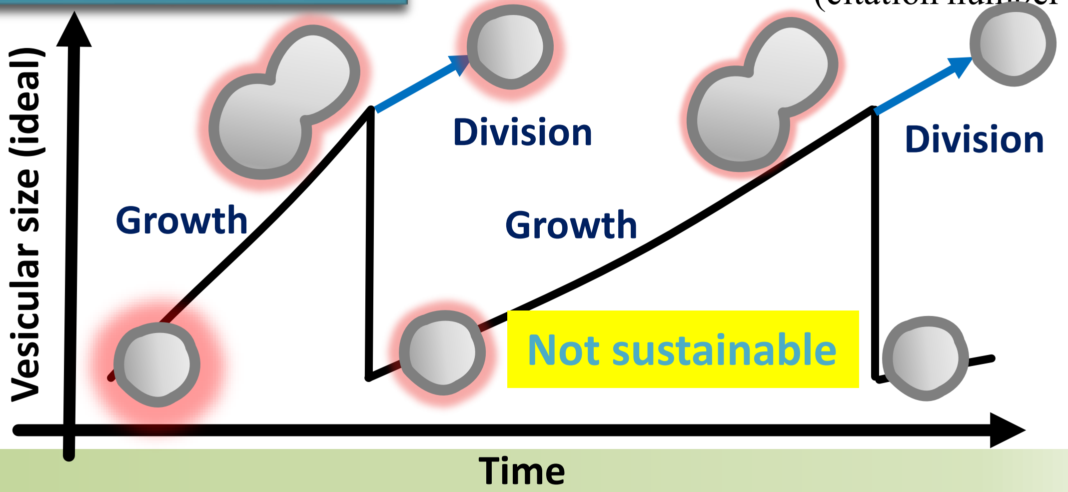
- **Reaction kinetics increase with vesicular growth.**
- **Reaction kinetics decrease due to vesicular division.**

Autocatalytic System



Non-autocatalytic System

e.g. Kurihara, Sugawara et al. *Nat. Chem.* (2011).
(citation number > 420)

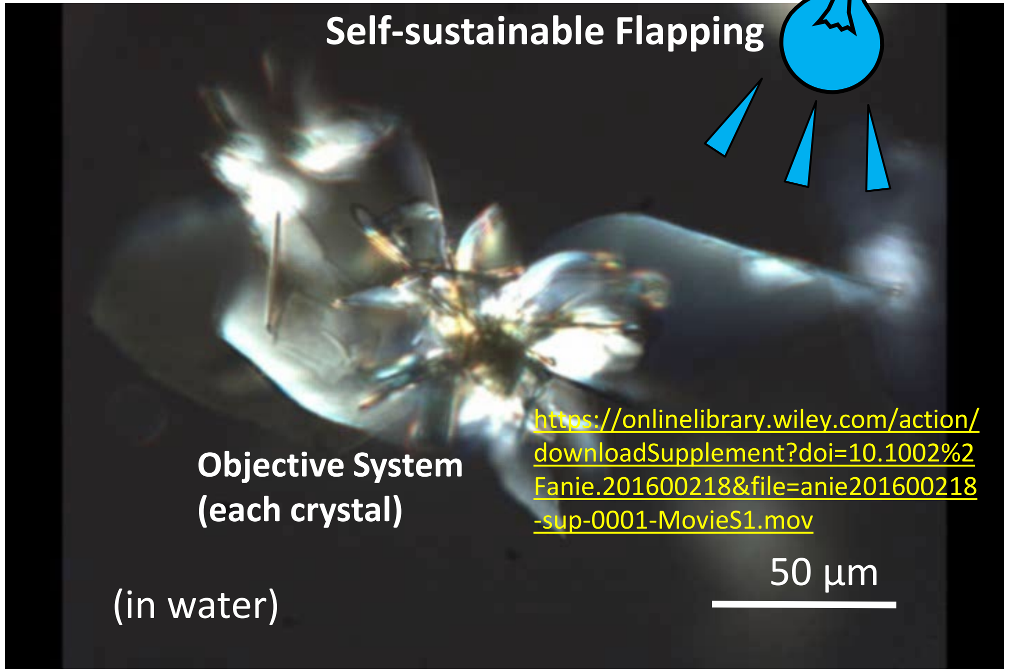


The highly cited paper has smaller meaning in Systems Chemistry.

Light-driven self-oscillation of crystal

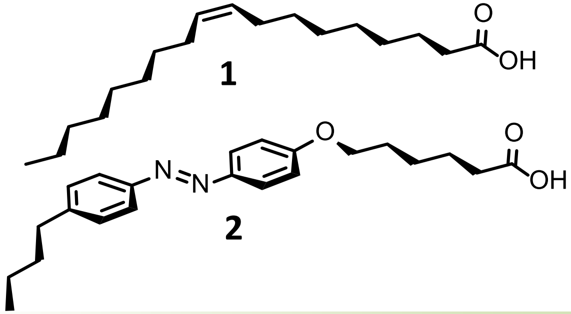
- *Trans*-to-*cis* reaction velocity decrease by the 1st phase transition
- *Trans*-to-*cis* reaction velocity increase by the 2nd phase transition

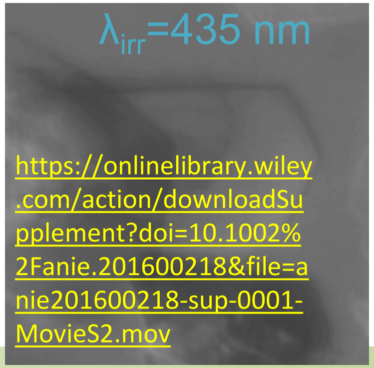
Continuous light irradiation



https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fanie.201600218&file=anie201600218-sup-0001-MovieS1.mov

T. Ikegami, et al. *Angew. Chem. Int. Ed.* 55, 8239-8243 (2016).
Y. Kageyama, et al. *Chem. Eur. J.* 26, 10759-10768 (2020).





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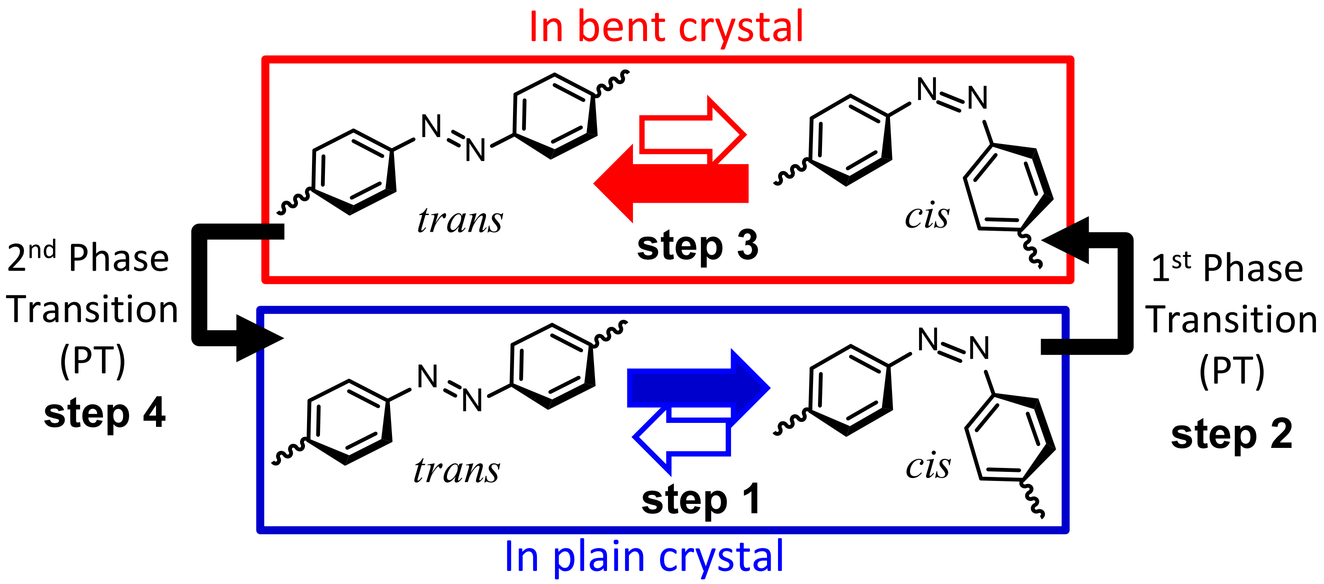
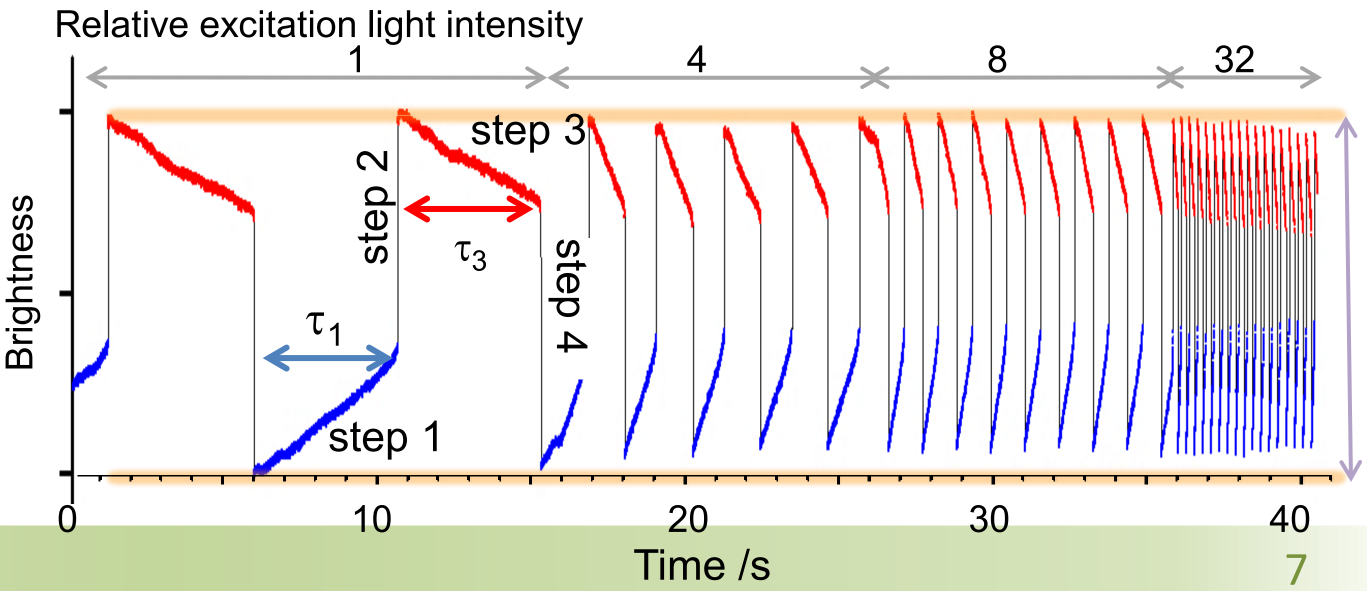
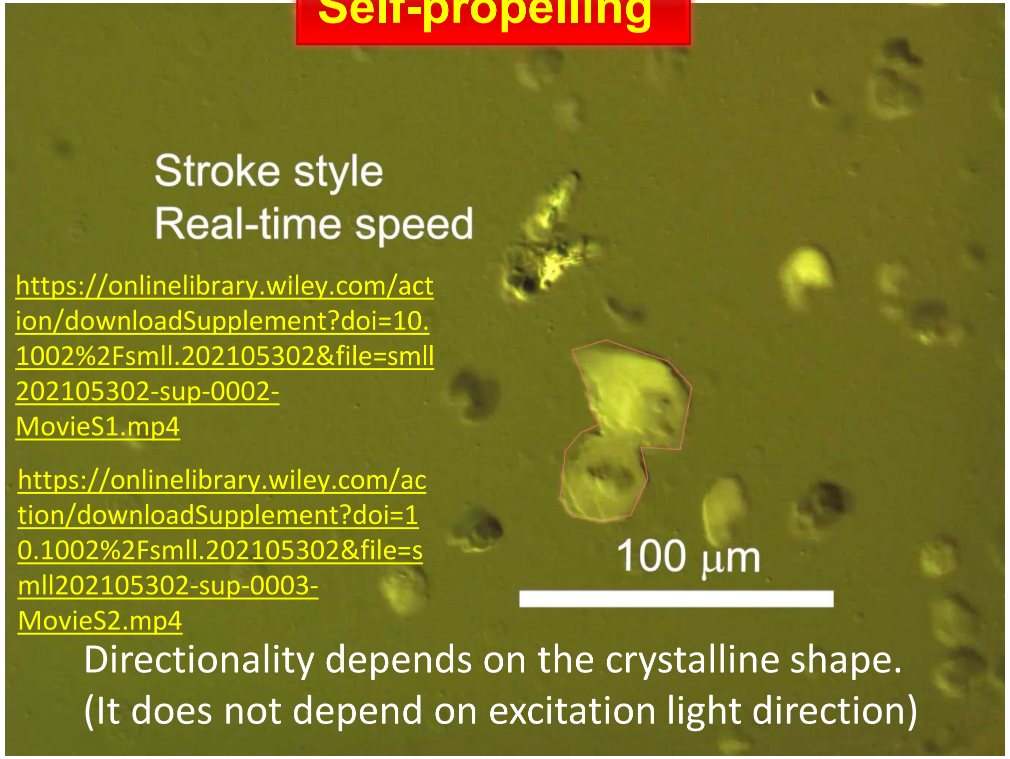




Life-like functions of light-driven self-oscillatory crystal

Self-propelling



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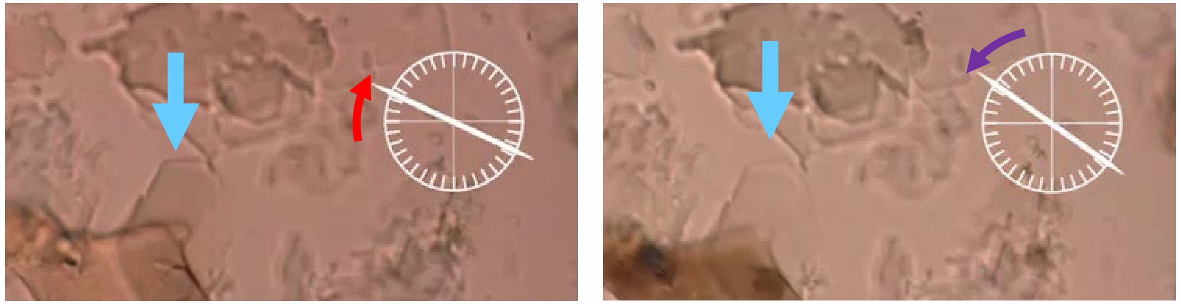
https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fsmll.202105302&file=smll202105302-sup-0003-MovieS2.mp4

Directionality depends on the crystalline shape.
(It does not depend on excitation light direction)

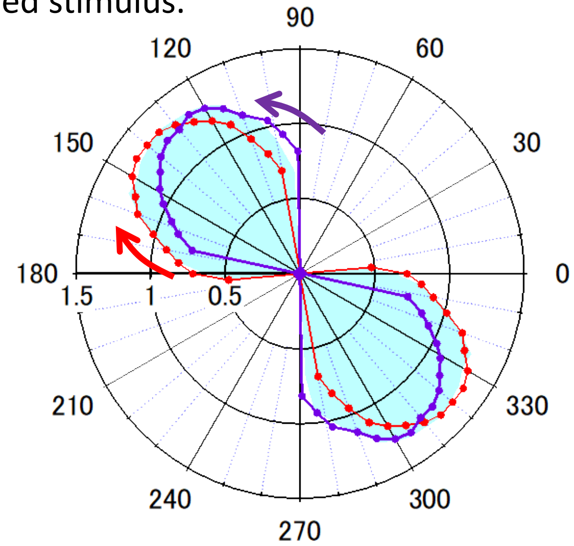
K. Obara, et al. *Small* 18, 2105302 (2022).

- Powerstroke due to multimolecular process (phase transition)
- Symmetry breaking in motion (exception of scallop theorem)

Memory effect



When the excitation light is polarized, the frequency changes with the direction of rotation of the polarization angle. The crystal remembers the previously received stimulus.



Y. Kageyama, et al. *arXiv* 2301.09873 (2023).

Note: Condition characterizes the behavior of the system.

Summary 1

Under energy flow condition, ensemble of molecules

Non-equilibrium chemical system

Equilibrated behavior

Composition becomes apparently constant.

Catalytic/photocatalytic reactions

Molecular-level motors
[Nobel Prize in Chemistry 2016]

Light-responsive materials

Vesicular self-reproduction
[Sugawara, *Nat. Chem.* 2011; *Nat. Commun.* 2013, &s]

Dissipative self-assembly

Self-assembly in dissipative condition

Far-from-equilibrium behavior

Composition fluctuates.

Light-driven self-oscillatory & self-propulsive crystal
[Kageyama, *ACIE* 2016; *Small* 2022]

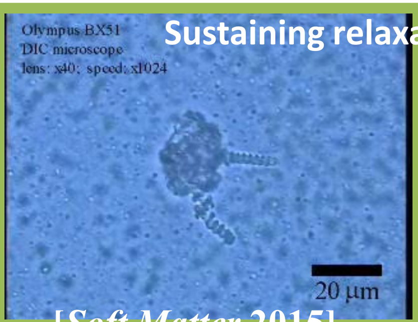
Autocatalytic vesicle reproduction (Self-replication)
[Takahashi, Sugawara, *ChemComm* 2010]
[Devaraj, *PNAS* 2015]

Self-oscillatory assembly
[Hermans *Nat. Nanotechnol.* 2018, Fletcher *Nat. Chem.* 2022]

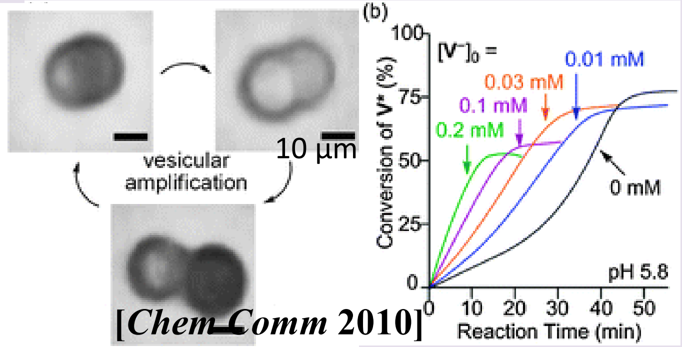
Behaviors difficult to classify due to the flamework of thermodynamics

1. **Sustainable relaxation dynamics that does not reach equilibrium** [Kageyama, *Soft Matter* 2015]
2. **Continuous behavior with self-shadowing mechanism due to the directionality of the energy resource** [Broer, *Nature* 2017]

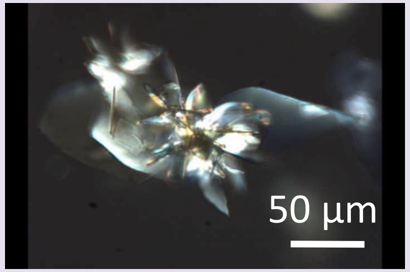
Sustaining relaxation



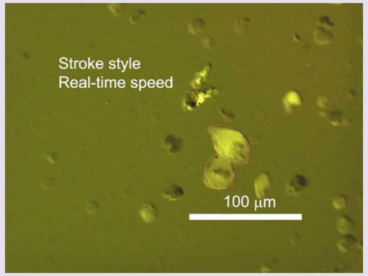
[*Soft Matter* 2015]



[*Chem Comm* 2010]



[*ACIE* 2016]



[*Small* 2022]

Summary 2 (Perspectives and Comments)

My perspectives:

Systems chemistry is an important research field that enables us to create life-like dynamics and gain insights into the intrinsic features of life.
Systems chemistry shows indeterministic behavior: this point is inherently different from supramolecular chemistry where molecular structure dominantly characterizes the feature of the objects.
The significance in systems chemistry is in its deviation from common perspectives in chemistry.

My concerns:

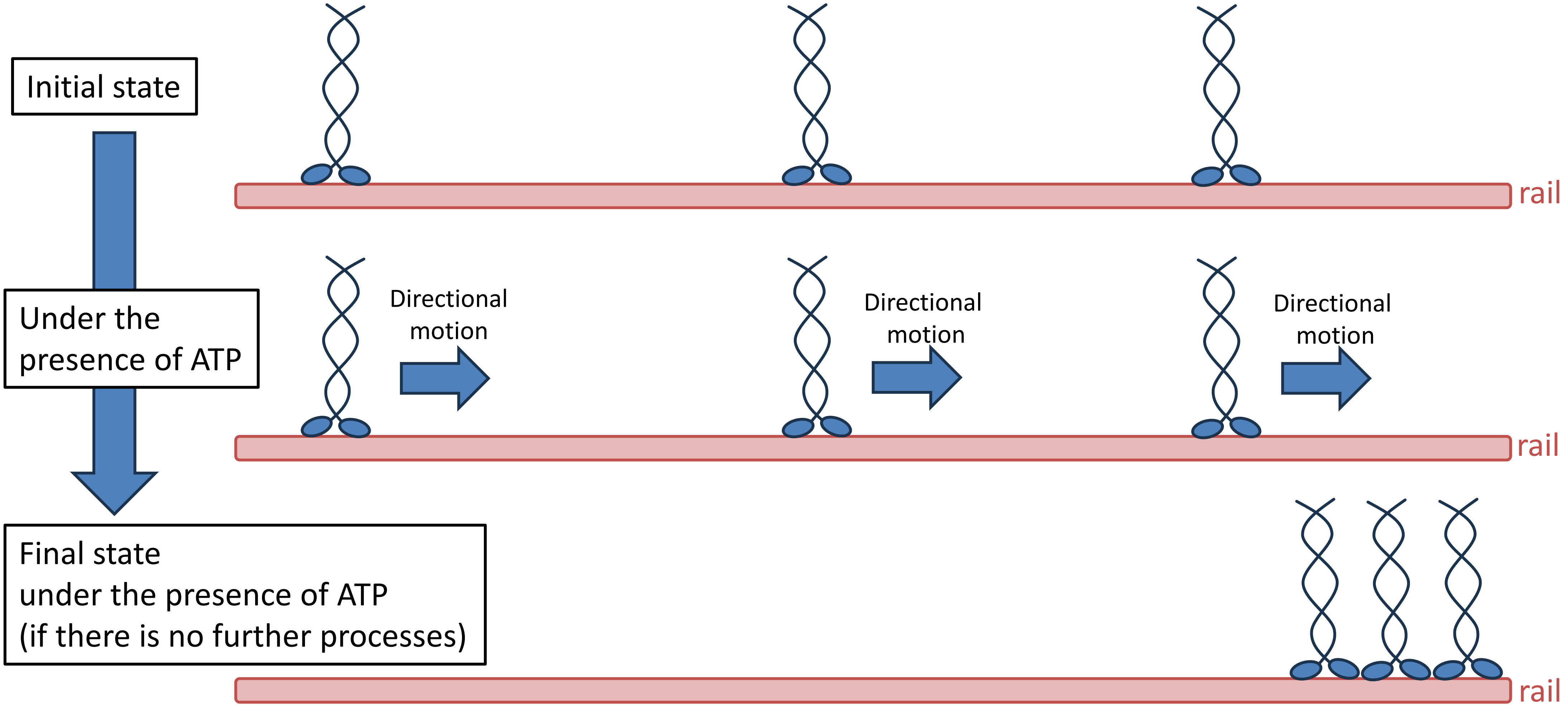
Currently, at embryo stage of systems chemistry, discussions ignoring the achievement in physical chemistry are more likely to be published and cited.
→ This trend must lead to the decline of this challenging and exciting field.
→ This trend must force young chemists to pay their efforts on non-essential research goals.

My proposals: they are no further from general ethics for scientists.

Science is a process of continually advancing while making mistakes and correcting them.
Accepting this fact and contributing for further development are the roles of scientists including students.
Specifically, I propose,

1. **When drawing graphs, be sure to indicate the axis labels** to prevent errors. Many papers in this field contain unclear potential curves.
2. **Respect diverse perspectives**, as systems chemistry is a multidisciplinary area of chemistry.
3. **Do not blindly trust journal reputation**: Quantitative evaluations reflect the world's situation but do not guarantee legitimacy.
4. **Consider what we leave behind for the next generation**: Researches for temporary fame are not creative.

We know breaking microscopic reversibility shifts the distribution.



Initial state

Under the
presence of ATP

Final state
under the presence of ATP
(if there is no further processes)

Breaking of microscopic reversibility results in a distribution shift.
The behavior of the distribution shift is up-hill relaxation* but not far-from-equilibrium.

(If the rail extends infinitely or is circular, the molecules may operate eternally, even though it is not far from equilibrium.)

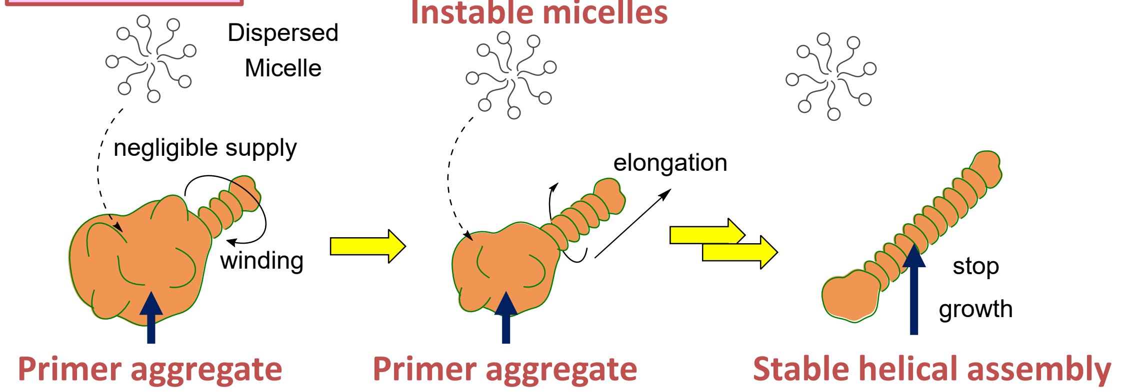
* up-hill relaxation: relaxation process that transitions a system towards a likely state, resulting in an increase in the internal energy of the system.

Continuous dynamics is not only in far-from-equilibrium

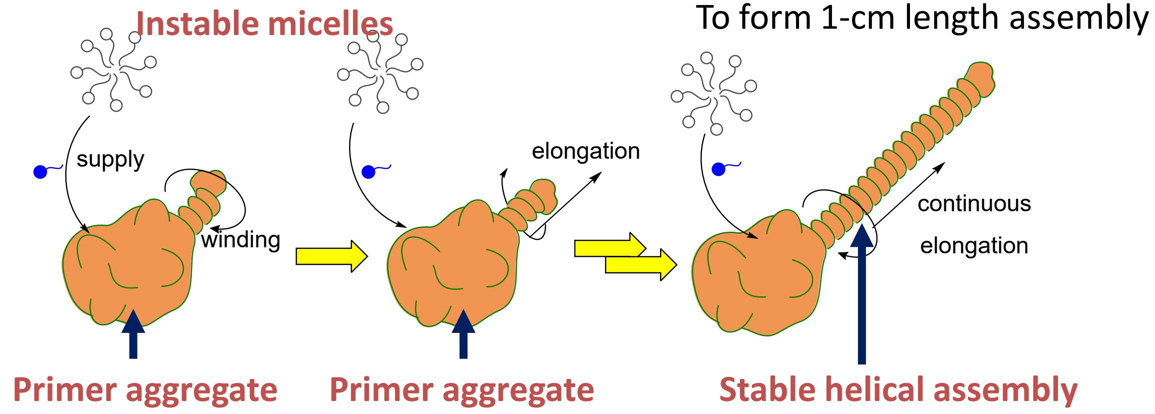
We can observe dynamics while relaxation process.

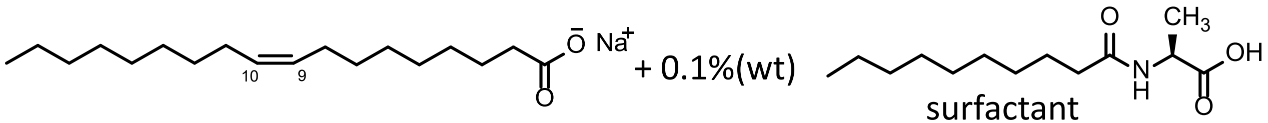
If the span of the relaxation process becomes eternal, we can observe continuous mechanical dynamics.

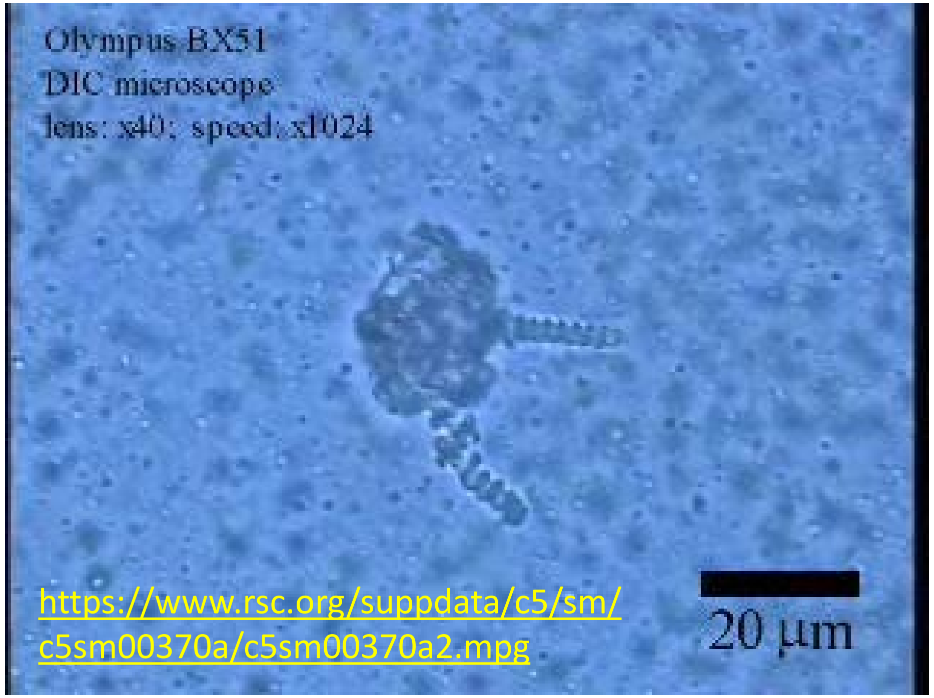
Non additive



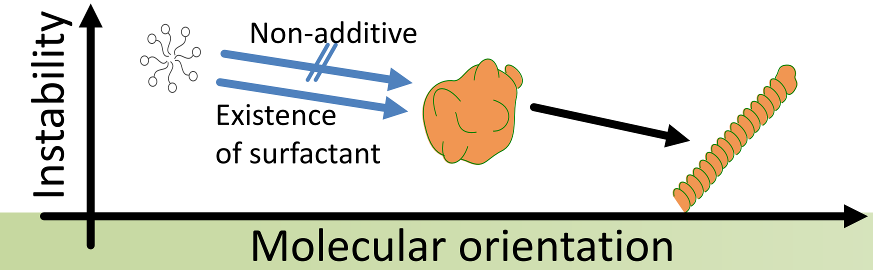
In the presence of surfactant





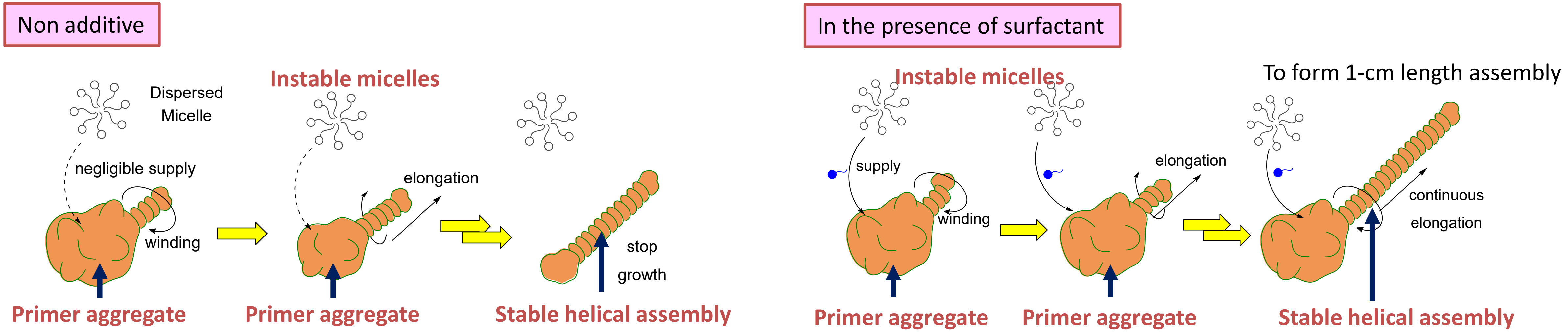


https://www.rsc.org/suppdata/c5/sm/c5sm00370a/c5sm00370a2.mpg



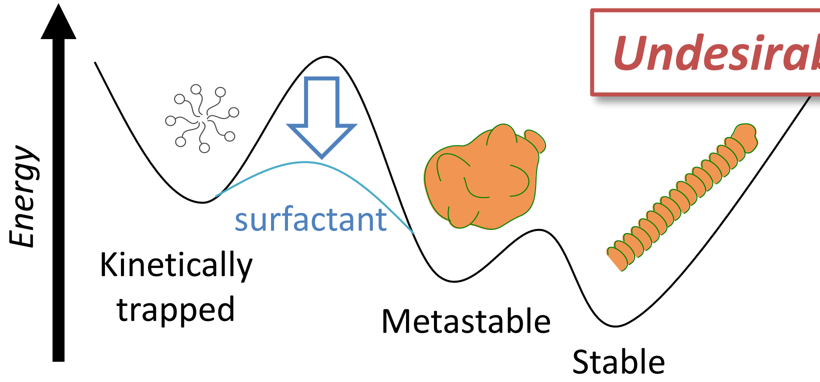
Kageyama et al. *Soft Matter*, 11, 3550-3558 (2015).

Molecular assembly proceeds step-by-step



If we had drawn a picture like the one below, it would be more intuitive to the readers and the paper might have been more attractive. However, the diagram below is incorrect in chemical thermodynamics.

We are now facing to a conflict problem of sensory clarity taking precedence over academic accuracy.



Undesirable figure

Reasons why it is undesirable:

[If the figure is for a reaction coordinate]

1. We should illustrate the transition structures (saddle-point structures).
2. We should illustrate unifying the components including water of hydration.
3. Another reasons, read **https://arxiv.org/abs/2211.06147**

[If the figure is for the total energy of a system]

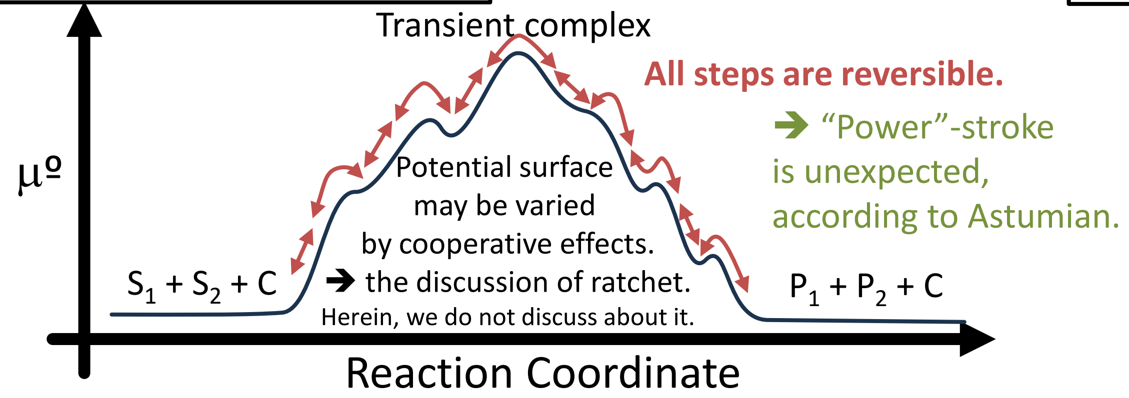
1. We cannot illustrate activation energy as shown in energy-landscape.
2. Another reasons, read **https://arxiv.org/abs/2211.06147**

Kageyama et al. *Soft Matter*, **11**, 3550-3558 (2015).

photochemical process is special” is for microscopic reversibility

Regarding molecular level behavior ➔ It is very different from a thermal chemical process.

Thermal reaction process

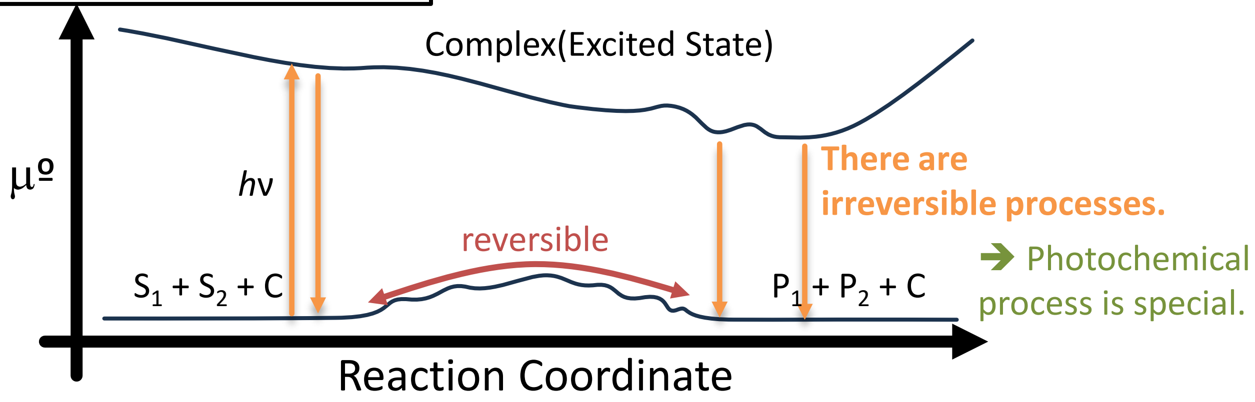


All steps are reversible.

➔ “Power”-stroke is unexpected, according to Astumian.

Potential surface may be varied by cooperative effects.
➔ the discussion of ratchet.
Herein, we do not discuss about it.

Photochemical process

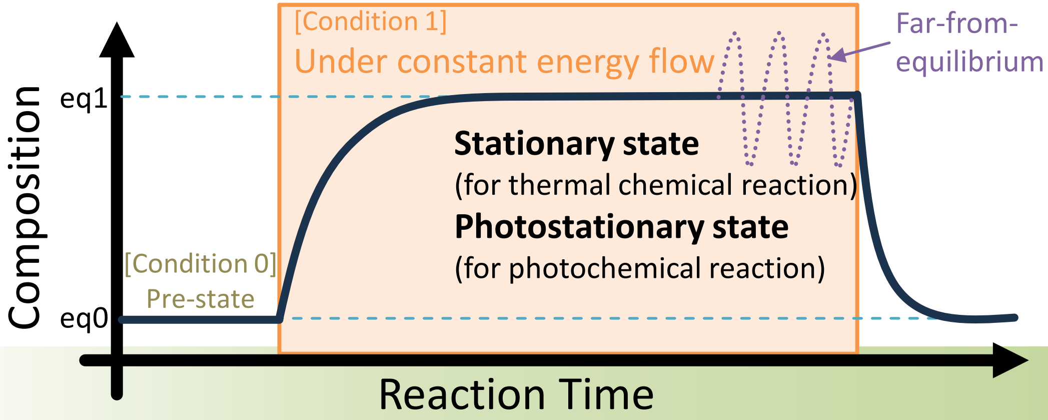


There are irreversible processes.

➔ Photochemical process is special.

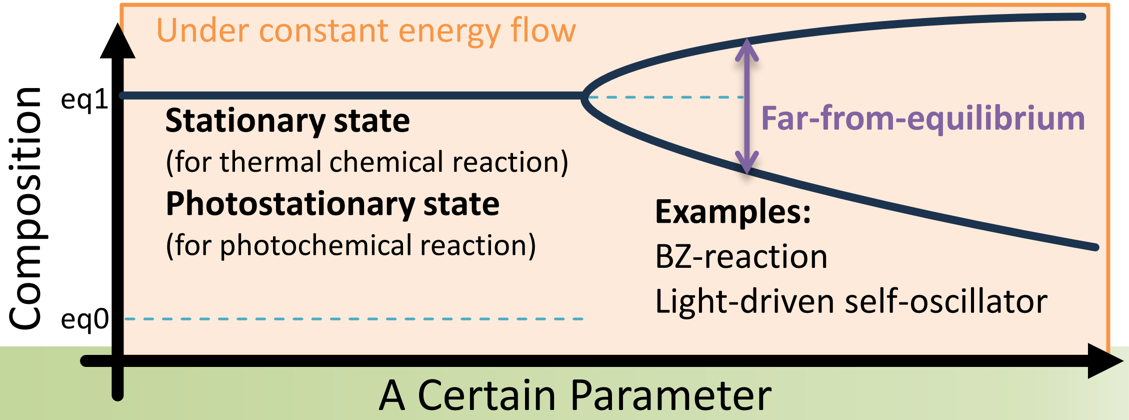
Regarding system behavior ➔ The key issue is same. ➔ Photochemical process is not so special.

Time profile of reaction (product curve)



Stationary state (for thermal chemical reaction)
Photostationary state (for photochemical reaction)

Bifurcation diagram

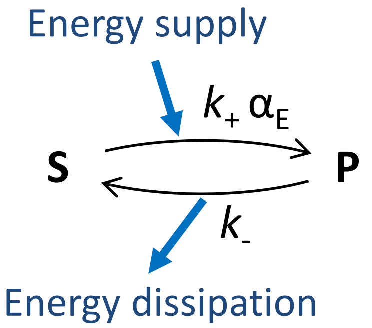


Stationary state (for thermal chemical reaction)
Photostationary state (for photochemical reaction)

Examples:
BZ-reaction
Light-driven self-oscillator

Consider simply

Reaction scheme



Reaction velocities

$$v_+ = k_+ \alpha_E [S]$$

$$v_- = k_- [P]$$

Ratio of the components

$$\frac{[P]}{[S]} = \frac{k_+ \alpha_E}{k_-}$$

α_E : Apparent density of receiving energy
k_+, k_- : Apparent reaction kinetic constants

System becomes equilibrium under constant energy supply

$\frac{[P]}{[S]}$: **Constant**

Far-from-equilibrium system where composition fluctuate

$\frac{[P]}{[S]}$: **Fluctuate**

How to design a self-continuous system:

Strategy 1: Fluctuation of α_E (apparent density of receiving energy)

Strategy 2: Fluctuation of k_+ and/or k_- (apparent kinetic constants)

If the fluctuations occur with internal phenomena, the system can be regarded as autonomous.
We can fluctuate the parameters externally: but we should not regard it as autonomous.

The term of “feedback” is common but somewhat difficult to understand. The key is fluctuation in kinetic constants.