Beyond Boltzmann:
A brief Intro to Dissipative Systems by Example

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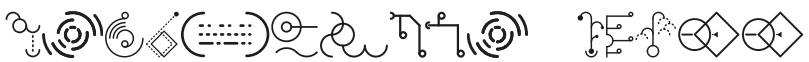

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Molecular walker based on the kinsin motor

$$\text{Back} \quad E_b + \text{ATP} \underset{k_{-\text{ATP},b}}{\overset{k_{+\text{ATP},b}}{\rightleftharpoons}} \text{E(ATP} \rightleftharpoons \text{ADP} \bullet P_i) \underset{k_{+\text{ADP},b}}{\overset{k_{-\text{ADP},b}}{\rightleftharpoons}} E_b + \text{ADP} + P_i$$

$$\text{Front} \quad E_f + \text{ATP} \underset{k_{-\text{ATP},f}}{\overset{k_{+\text{ATP},f}}{\rightleftharpoons}} \text{E(ATP} \rightleftharpoons \text{ADP} \bullet P_i) \underset{k_{-\text{ADP},f}}{\overset{k_{+\text{ADP},f}}{\rightleftharpoons}} E_b + \text{ADP} + P_i$$

$\rightleftharpoons$ fast reaction rate

$\rightleftharpoons$ slow reaction rate

The specificity for ATP/ADP binding differs on front and back head.

Specificity switching is implemented physically via strain between the neck linker and the ATPase active site.

Figure modified from Astumian RD (2012), Microscopic reversibility as the organizing principle of molecular machines; *Nature Nanotech* **7**:684-688 | doi:10.1038/nnano.2012.188

Synthetic electrochemical analogue (stochastic pump)

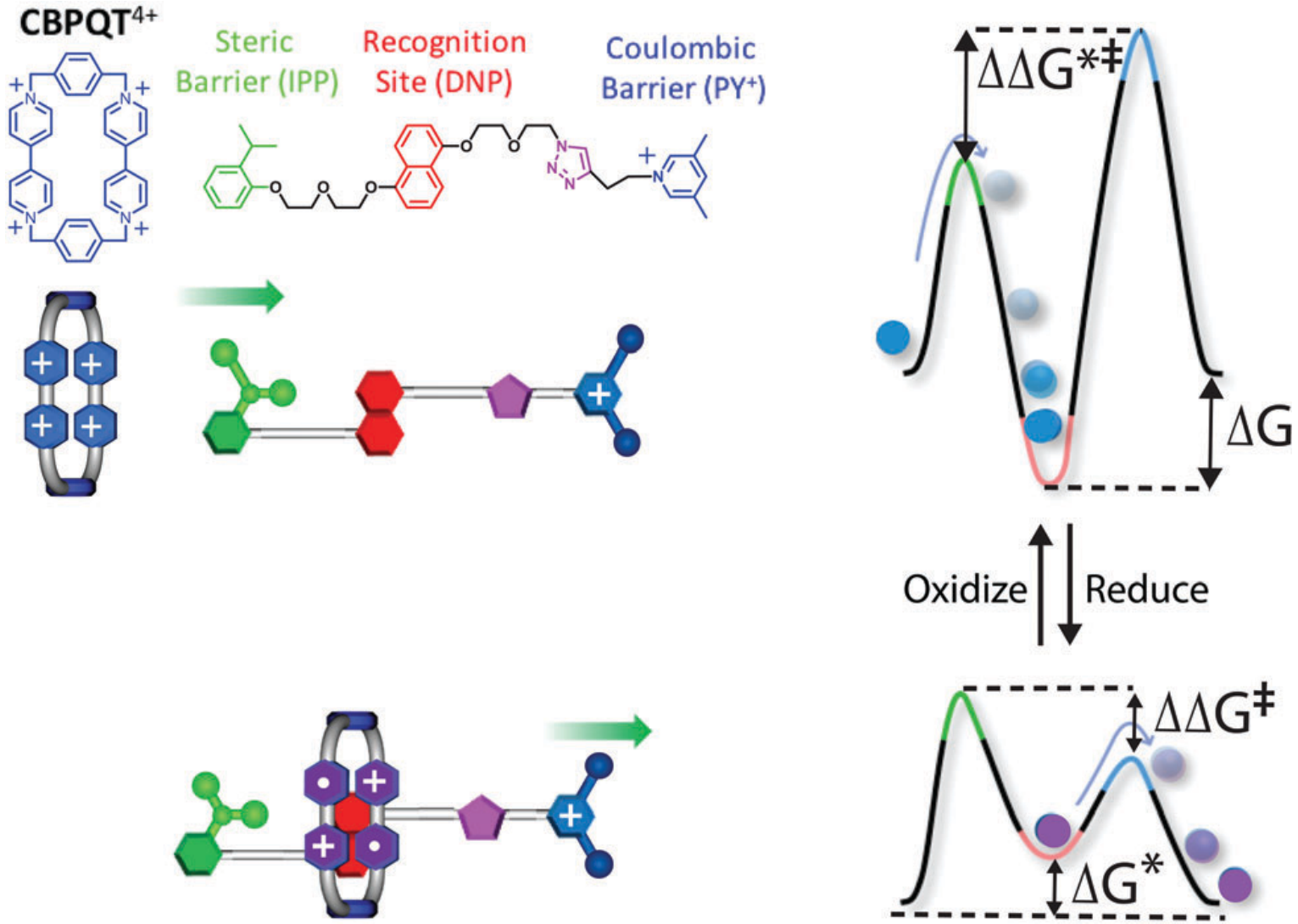
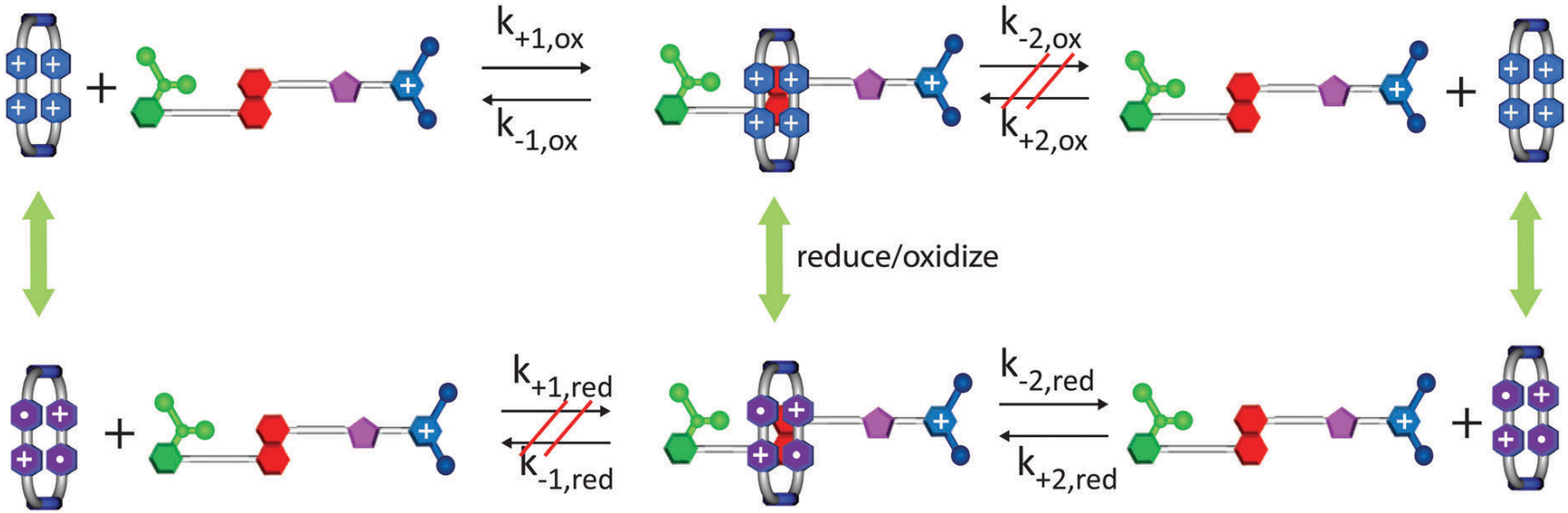


Figure modified from Astumian RD (2018), Stochastic pumping of non-equilibrium steady-states: how molecules adapt to a fluctuating environment; *Chem Comm* **54**:427-444 | doi:10.1039/c7cc06683j

Kinetic Mechanism for unidirectional threading

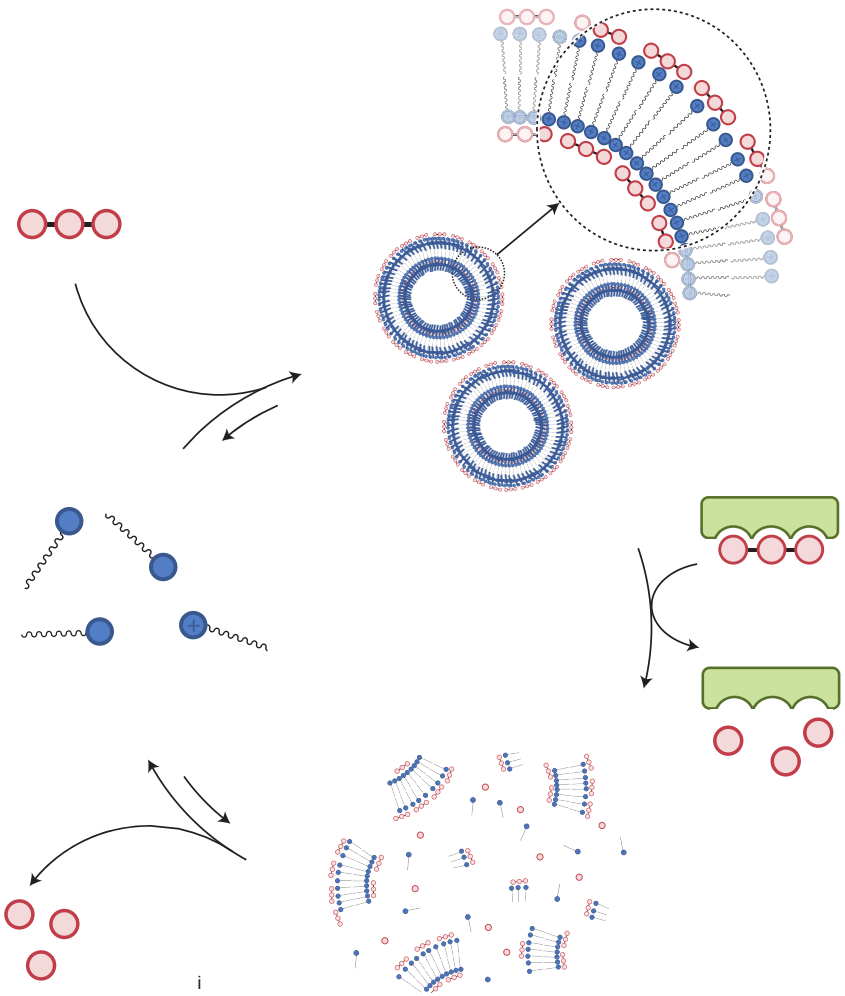


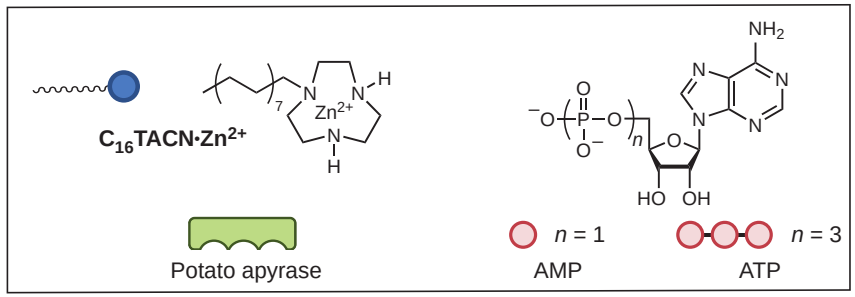
By design the kinetic specificities obey

$$k_{+1,\mathrm{ox}}/k_{+2,\mathrm{ox}} \gg 1 \qquad \text{and} \qquad k_{-2,\mathrm{red}}/k_{-1,\mathrm{red}} \gg 1$$

Figure modified from Astumian RD (2018), Stochastic pumping of non-equilibrium steady-states: how molecules adapt to a fluctuating environment; *Chem Comm* **54**:427-444 | doi:10.1039/c7cc06683j

Self-assembly under dissipative conditions

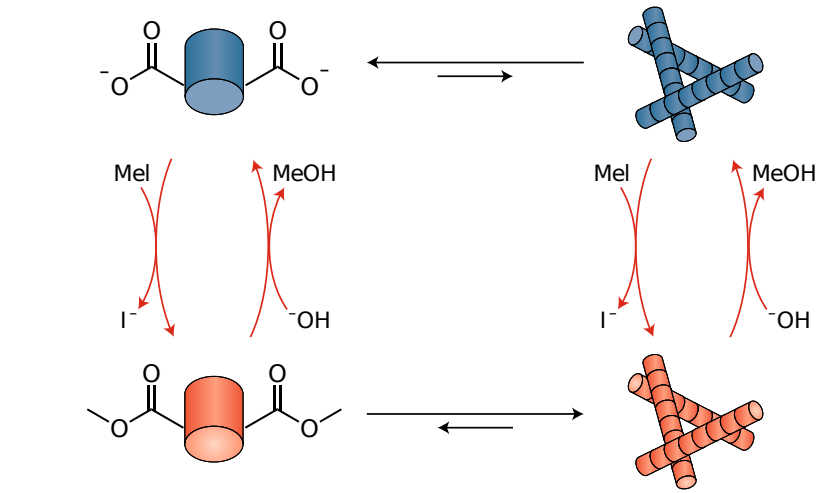


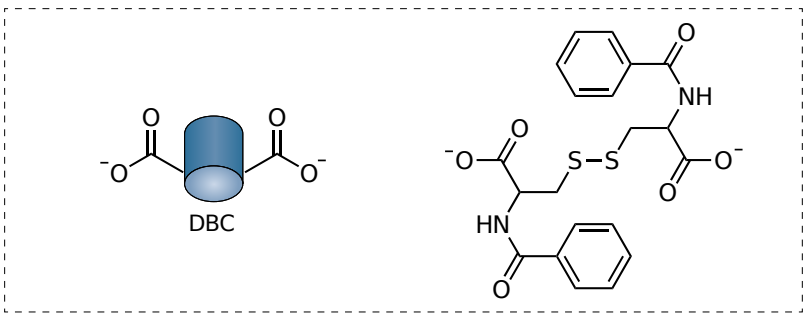


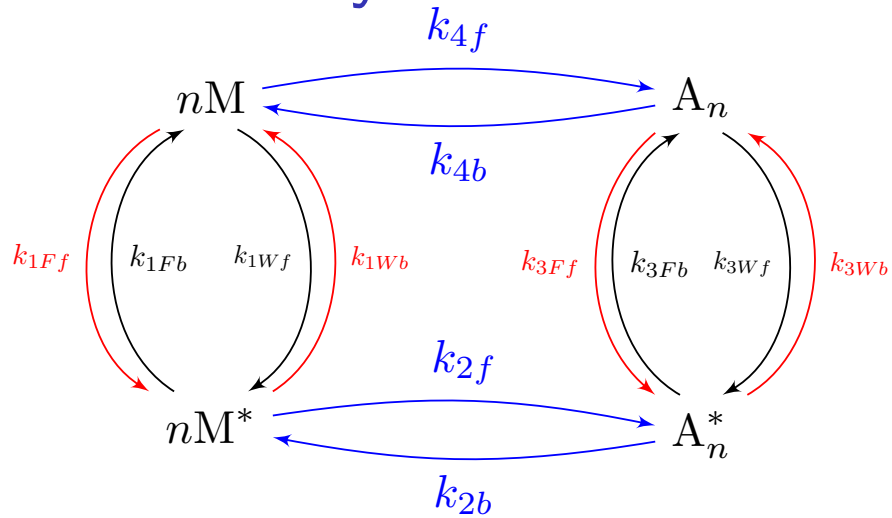
1. Vesicles form way below the critical aggregation concentration.
2. System adapts in a Le Châtelier-like manner.
3. Monomers / assemblies are not involved in fuel-to-wast conversion.
4. All consumed energy is just dissipated.

Figure modified from Maiti S et al (2016),Dissipative self-assembly of vesicular nanoreactors; *Nature Chem* **8**:725-731 | doi:10.1038/nchem.2511

Dissipative self-assembly







$$\underbrace{\left(\frac{k_{1Ff}+k_{1Wf}}{k_{1Wb}+k_{1Fb}}\right)^{n}}_{K_1}\cdot K_2\cdot\underbrace{\left(\frac{k_{3Ff}+k_{3Wf}}{k_{3Wb}+k_{3Fb}}\right)^{-1}}_{K_3^{-1}}\cdot K_4^{-1}=K_r$$

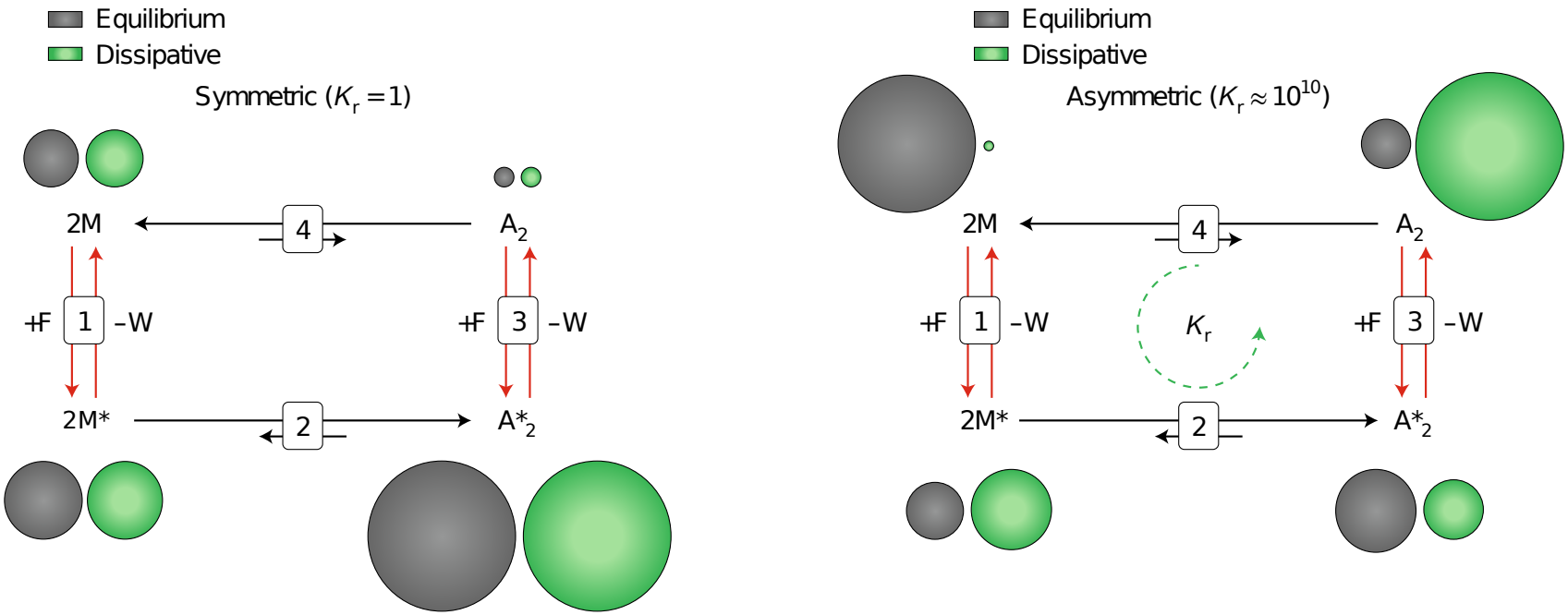
Rachting constant $K_r = 1$ no directional preference for cycling.

$K_r > 1$ preference for counterclockwise cycling.
(Fuel preferentially activates M as opposed to A_2).

(Waste production is kinetically favored from state A_2^*)

Figure modified from Ragazzon G & Prins LJ (2018), Energy consumption in chemical fuel-driven self-assembly; *Nature Nanotech* **13**:882-888 | doi:10.1038/s41565-018-0250-8

Kinetic asymmetry drives the system out of equilibrium

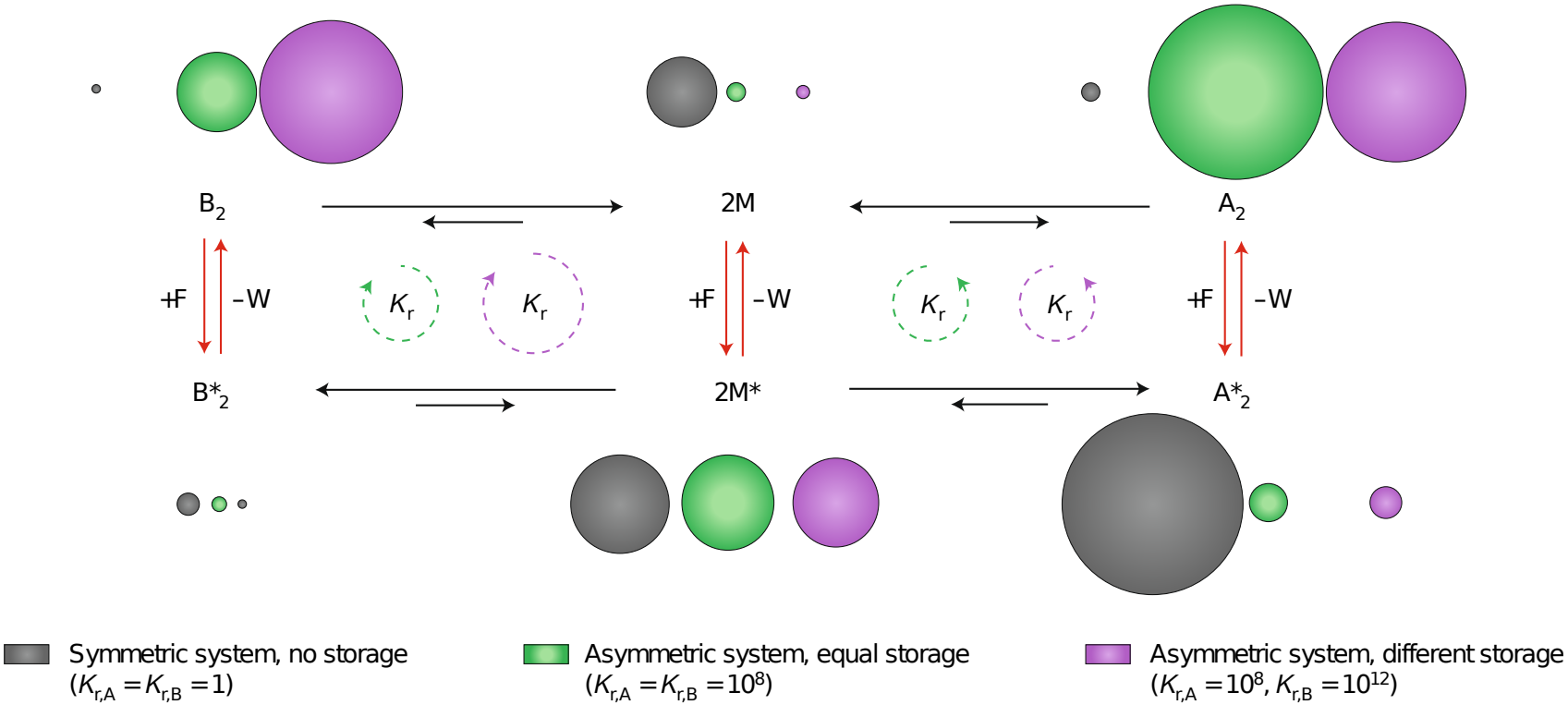


A certain amount of energy is stored in the system under stationay dissipative conditions.

The ratcheting constent quantifies to which extent the system is driven out of equilibrium.

Figure modified from Ragazzon G & Prins LJ (2018), Energy consumption in chemical fuel-driven self-assembly; *Nature Nanotech* **13**:882-888 | doi:10.1038/s41565-018-0250-8

Selection in the case of competing dissipative pathways



B_2 is trmodynamically less stable than A_2.

Is the most dissipative state selected ("dissipative adaption")?

1. Kinetic asymmetry in energy consumption is required.
2. Ratcheting strength can dominate over relative TD stabilities.

Figure modified from Ragazzon G & Prins LJ (2018), Energy consumption in chemical fuel-driven self-assembly; *Nature Nanotech* **13**:882-888 | doi:10.1038/s41565-018-0250-8

Further Reading

Astumian RD

Trajectory and Cycle-Based Thermodynamics and Kinetics of Molecular Machines: The Importance of Microscopic Reversibility. *Acc Chem Res*, **51**:2653-2661 (2018) | doi:10.1021/acs.accounts.8b00253

Astumian RD

Stochastic Conformational Pumping: A Mechanism for Free-Energy Transduction by Molecules. *Annu Rev Biophys* **40**:289-313 (2011) | doi:10.1146/annurev-biophys-042910-155355

Boekhoven J, Brizard AM, Kowlgi KNK, Koper GJM, Eelkema R, van Esch JH

Dissipative Self-Assembly of a Molecular Gelator by Using a Chemical Fuel. *Angew Chem Int Ed*, **49**:4825-4828 (2010) | doi:10.1002/anie.201001511

Del Grosso E, Ragazzon G, Prins L, Ricci F

Fuel-responsive allosteric DNA-based aptamers for the transient release of ATP and cocaine. *Angew Chem Int Ed*, *accepted article* (2019) | doi:10.1002/anie.201812885

della Sala F, Neri S, Maiti S, Chen JL-Y,Prins JL

Transient self-assembly of molecular nanostructures driven by chemical fuels. *Curr Opin Biotech*, **46**:27-33 (2017) | doi:10.1016/j.copbio.2016.10.014

Zhang L, Marcos V, Leigh DA

Molecular machines with bio-inspired mechanisms. *PNAS*, **115**(38):9397-9404 (2018) | doi:10.1073/pnas.1712788115