

Self-assembly of dimer systems

Analytical results

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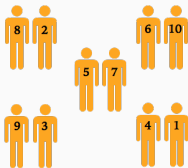
May 15, 2018

Shakhnovich Group Meeting

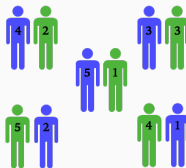
A Mathematical Primer

A question of combinatorics

Say we have two systems



(a) Non-gendered dancers



(b) Gendered dancers

We want to ask two purely combinatorics questions about these two systems:

- **System of gendered partners:** We have N male-female couples together in a dance hall. The members of the couples separate. How many ways can we form $k \leq N$ couples such that *none* of these couples are from the original set?
- **System of nongendered partners:** We have N couples together in a dance hall. The members of the couple separate. How many ways can we form $k \leq N$ couples such that *none* of these couples are from the original set?

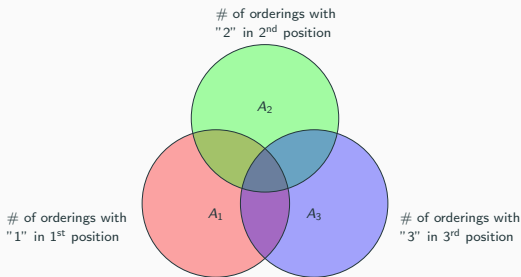
These questions are relevant to specific and non-specific interactions between biomolecules. We can use the principle of inclusion/exclusion to answer this question.

But first, it's best to work through a simpler example.

Example: Permutations of (1, 2, 3)

Question: What is the number of ways to order the numbers 1, 2, 3, such that *no* number k is in its k th position? (We define this number as d_3)

Answer: The total size of the set of all permutations is $3!$. Let A_k be the set of all permutations where k is in the k th position. The desired quantity d_3 is the number of elements in the complement of the union of A_1 , A_2 , and A_3 .



Namely,

$$d_3 = 3! - |A_1 \cup A_2 \cup A_3|,$$

where $|S|$ is the size of the set S .

Example: Permutations of (1, 2, 3), continued

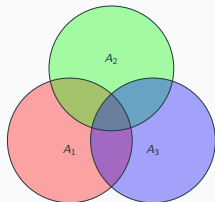
We want to find

$$d_3 = 3! - |A_1 \cup A_2 \cup A_3|,$$

where $|S|$ is the size of the set S , and A_k be the set of all permutations where k is in the k th position.

We compute the quantity d_3 , by inspecting the figure and writing the *union* of the three sets as sums and differences between the intersection between the sets.

We note that



$$\begin{aligned} |A_1 \cup A_2 \cup A_3| &= |A_1| + |A_2| + |A_3| \\ &\quad - |A_1 \cap A_2| - |A_2 \cap A_3| - |A_3 \cap A_1| \\ &\quad + |A_1 \cap A_2 \cap A_3| \\ &= 3(3-1)! - 3(3-2)! + 1(3-3)! \end{aligned}$$

Thus our desired result is

$$d_3 = 3! - 3(3-1)! + 3(3-2)! - 1(3-3)! = 2$$

This is basic way we handle these "no element in the 'correct' place" problems. (The foundational principle is called "the principle of inclusion and exclusion")

The previous answer was simple. However, the exact answer to this example is not important. The *method* is what is significant.

We can rewrite our answer as

$$d_3 = 3! - 3(3-1)! - 3(3-2)! + 1(3-3)! = \sum_{j=0}^3 (-1)^j \binom{3}{j} (3-j)!.$$

This result suggests a generalization:

Derangement (def.) *The number of ways to order the numbers $1, 2, \dots, N$ such that no number k is in the k th position is*

$$d_N = \sum_{j=0}^N (-1)^j \binom{N}{j} (N-j)!.$$

What is important in the equation for d_N is that the $j = 0$ term is the number of ways to order all the numbers without constraint.

Back to dancing couples

With this method we can now answer our original combinatorics questions

Non-gendered partners problem

Total number of possible pairs

The number of ways to form k pairs from $2N$ non-gendered elements is

$$\binom{2N}{2k} (2k - 1)!!.$$

Answer to Q on slide

The number of ways to form k pairs from $2N$ non-gendered *such that none of the pairs were part of some original pairing* is

$$a_{N,k} = \sum_{j=0}^N (-1)^j \binom{N}{j} \binom{2N-2j}{2k-2j} (2k-2j-1)!!$$

Gendered partners problem

Total number of possible pairs

The number of ways to form k male-female pairs from N males and N females is

$$\binom{N}{k}^2 k!.$$

Answer to Q on slide

The number of ways to form k male-female pairs from N males and N females *such that none of the pairs were part of some original pairing* is

$$b_{N,k} = \sum_{j=0}^N (-1)^j \binom{N}{j} \binom{N-j}{k-j}^2 (k-j)!$$

Non-gendered Partition Function

Properties of the **non-gendered** dimer system

We want to compute the partition function (and ultimately the equilibrium constraints) for a system of **non-gendered** monomers which can form correct and incorrect dimers.

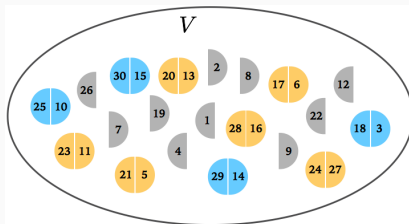


Figure 2: This microstate has four favorable contacts (in blue), six unfavorable contacts (in yellow), and ten unpaired subunits (in grey) and has an energy $-(10E_0 + 4\Delta)$.

We have monomers α_k for $k = 1, \dots, N, N+1, \dots, 2N$ which are distinct and exist as single copies. If two α monomers come into contact (say an α_i and an α_j monomer) the two can form a dimer with binding energy

$$\mathcal{E}(\alpha_i, \alpha_j) = \begin{cases} -(E_0 + \Delta) & \text{if } |i - j| = N, \\ -E_0 & \text{otherwise.} \end{cases}$$

The correct contacts are those for which α_1 binds with α_{N+1} , α_2 binds with α_{N+2} , and so on. The incorrect contacts are all other bindings.

Properties of the **non-gendered** dimer system

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$$\mathcal{E}(\alpha_i, \alpha_j) = \begin{cases} -(E_0 + \Delta) & \text{if } |i - j| = N, \\ -E_0 & \text{otherwise.} \end{cases}$$

The resulting partition function is

$$Z_N(\beta E_0, \beta \Delta) = \sum_{k=0}^N \sum_{m=0}^k \left(\frac{V}{\lambda_0^3} \right)^{2N-2k} \left(\frac{V}{(\lambda_0/\sqrt{2})^3} \right)^k e^{\beta E_0(k-m)} e^{\beta(E_0+\Delta)m} \binom{N}{m} a_{N-m, k-m},$$

where

$$a_{N,k} = \sum_{j=0}^N (-1)^j \binom{N}{j} \binom{2N-2j}{2k-2j} (2k-2j-1)!!,$$

and λ_0 is the de Broglie wavelengths for a monomer.

Partition function for **non-gendered** system

...with some identities we find...

The partition function for the **non-gendered dimer system** with a binding energy of E_0 for unfavorable pairs and a binding energy of $E_0 + \Delta$ for favorable pairs (where each monomer has mass m_0) is

$$Z_N(\beta E_0, \beta \Delta) = \frac{1}{2\sqrt{\pi} \Gamma(N + 1/2)} \left(\frac{V}{\lambda_0^3} \right)^{2N} \int_0^\infty dx dy \frac{e^{-x-y}}{\sqrt{xy}} \left(\mathcal{M}_+^{2N} + \mathcal{M}_-^{2N} \right),$$

where

$$\mathcal{M}_\pm \equiv \sqrt{x} \pm \left(\frac{2\sqrt{2}\lambda_0^3}{V} \right)^{1/2} e^{\beta E_0/2} \sqrt{y\Phi(x; \beta \Delta)},$$

with

$$\Phi(x; \beta \Delta) \equiv e^{\beta \Delta} + 2x - 1.$$

Here $\lambda_0 = h/\sqrt{2\pi m_0 k_B T}$ and m_0 is the mass of a monomer.

From this partition function, we can compute the equilibrium values of the **number of total dimer contacts** $\langle k \rangle$ and the **number of favorable dimer contacts** $\langle m \rangle$ with the definitions

$$\langle k \rangle = \frac{\partial}{\partial(\beta E_0)} \ln Z_N(\beta E_0, \beta \Delta), \quad \langle m \rangle = \frac{\partial}{\partial(\beta \Delta)} \ln Z_N(\beta E_0, \beta \Delta)$$

Equilibrium for **non-gendered** system

The previous partition function appears intractable, but we can simplify it greatly using Laplace's method (also known, as the method of steepest descent or the saddle point approximation).

We rewrite the partition function as

$$Z_N(\beta E_0, \beta \Delta) = \int_0^\infty dx dy \exp \left[-\beta F_N(x, y; \beta E_0, \beta \Delta) \right] \\ \simeq c_{0,N} \exp \left[-\beta F_N(\bar{x}, \bar{y}; \beta E_0, \beta \Delta) \right],$$

where βF_N is an **approximate free energy** for the system, and \bar{x} and \bar{y} are the values of x and y which give βF_N a local minimum.

Namely,

$$\partial_i (\beta F_N(x, y; \beta E_0, \beta \Delta)) \Big|_{x=\bar{x}, y=\bar{y}} = 0, \quad \det H_{ij} > 0, \quad \text{Tr } H_{ij} > 0,$$

where

$$H_{ij} = \partial_i \partial_j (\beta F_N(x, y; \beta E_0, \beta \Delta)) \Big|_{x=\bar{x}, y=\bar{y}},$$

is the Hessian matrix of the system.

With this approximation, we find the equilibrium conditions

$$\frac{4\sqrt{2}\lambda_0^3}{V} e^{\beta E_0} = \frac{\langle k \rangle - \langle m \rangle (1 - e^{-\beta \Delta})}{(N - \langle k \rangle)^2}, \quad \frac{e^{\beta \Delta}}{2} = \langle m \rangle \frac{N - \langle m \rangle (1 - e^{-\beta \Delta})}{\langle k \rangle - \langle m \rangle (1 - e^{-\beta \Delta})}.$$

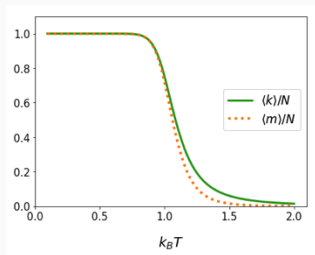
Type I and Type II dimer systems

From these equilibrium conditions, we find that we can distinguish between two types of dimer system characterized by how the parameters Δ , E_0 , λ_0^3/V (parametrized through $(\beta E_0)^{3/2} = \lambda_0^3/V$) and N relate to one another:

Type I (Strong Favorability)

$$\frac{\Delta}{\ln(2N)} > \frac{2}{3} \frac{E_0 + \Delta}{W_0 \left(\frac{2}{3} \frac{E_0 + \Delta}{E_V} \left(\frac{N}{4\sqrt{2}} \right)^{2/3} \right)}$$

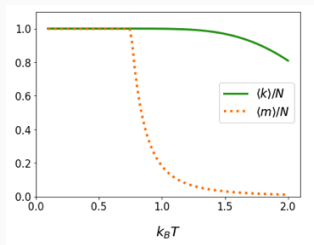
Example Plot



Type II (Weak Favorability)

$$\frac{\Delta}{\ln(2N)} < \frac{2}{3} \frac{E_0 + \Delta}{W_0 \left(\frac{2}{3} \frac{E_0 + \Delta}{E_V} \left(\frac{N}{4\sqrt{2}} \right)^{2/3} \right)}$$

Example Plot



*The function $W_0(x)$ is defined by $W_0(xe^x) = x$. These conditions are slightly corrected from my last group meeting.

Gendered Partition Function

Properties of the **gendered** dimer system

We want to compute the partition function (and ultimately the equilibrium constraints) for a system of **gendered** monomers which can form correct and incorrect dimers.

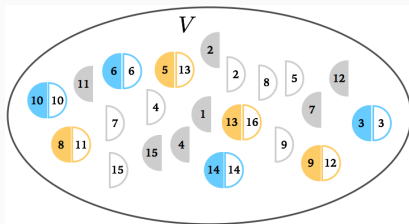


Figure 3: This microstate has four favorable contacts (in blue), six unfavorable contacts (in yellow), and ten unpaired subunits (in grey) and has an energy $-(10E_0 + 4\Delta)$.

We have monomers α_k for $k = 1, \dots, N$, and monomers β_k for $k = 1, \dots, N$. If an α monomer comes into contact with a β monomer, the two can form dimers (α_k, β_ℓ) with binding energy

$$\mathcal{E}(\alpha_i, \beta_j) = \begin{cases} -(E_0 + \Delta) & \text{if } i = j, \\ -E_0 & \text{otherwise.} \end{cases}$$

The correct contacts are those for which α_1 binds with β_1 , α_2 binds with β_2 , and so on. The incorrect contacts are all other bindings.

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$$\mathcal{E}(\alpha_i, \beta_j) = \begin{cases} -(E_0 + \Delta) & \text{if } i = j, \\ -E_0 & \text{otherwise.} \end{cases}$$

The resulting partition function is

$$Z_N(\beta E_0, \beta \Delta) = \sum_{k=0}^N \sum_{m=0}^k \left(\frac{V}{\lambda_\alpha^3} \right)^{N-k} \left(\frac{V}{\lambda_\beta^3} \right)^{N-k} \left(\frac{V}{\lambda_{\alpha\beta}^3} \right)^k e^{\beta E_0 k} \binom{N}{m} b_{N-m, k-m} e^{\beta \Delta m},$$

where

$$b_{N,k} = \sum_{j=0}^N (-1)^j \binom{N}{j} \binom{N-j}{k-j}^2 (k-j)!,$$

and λ_α , λ_β , and $\lambda_{\alpha\beta}$ are the de Broglie wavelengths for the α monomer, β monomer, and $\alpha\beta$ dimer respectively.

Partition function for **gendered** system

In a way similar to our analysis of the non-gendered system, we can analyze a gendered system.

We find that the partition function for the **gendered dimer system** with a binding energy of E_0 between unfavorable pairs and a binding energy of $E_0 + \Delta$ between favorable pairs (where one gender has mass m_α and the other has mass m_β) is

$$Z_N^{\text{gen.}}(\beta E_0, \beta \Delta) = \frac{1}{2\pi N!} \left(\frac{V}{\bar{\lambda}^3} \right)^{2N} \int_0^\infty dx dy \int_0^{2\pi} d\phi e^{-x-y} \mathcal{I}^N,$$

where

$$\mathcal{I} \equiv x + \frac{\lambda_\mu^3}{V} y \Omega(x; \beta \Delta) + 2 \left(\frac{\lambda_\mu^3}{V} \right)^{1/2} e^{\beta E_0/2} \sqrt{y \Omega(x; \beta \Delta)} \cos \phi,$$

with

$$\Omega(x; \beta \Delta) \equiv e^{\beta \Delta} + x - 1.$$

The quantities $\bar{\lambda}$ and λ_μ are the de Broglie thermal wavelengths computed from the geometric mean and the reduced mass, respectively, of the two species of monomers:

$$\bar{\lambda} = \frac{h}{\sqrt{2\pi k_B T (m_\alpha m_\beta)^{1/2}}}, \quad \lambda_\mu = \frac{h}{\sqrt{2\pi k_B T} \sqrt{\frac{1}{m_\alpha} + \frac{1}{m_\beta}}}$$

Equilibrium for **gendered** system

From the previous partition function, we can compute the equilibrium values of the **number of total dimer contacts** $\langle j \rangle$ and the **number of favorable dimer contacts** $\langle \ell \rangle$ with the definitions

$$\langle j \rangle = \frac{\partial}{\partial(\beta E_0)} \ln Z_N^{\text{gen.}}(\beta E_0, \beta \Delta), \quad \langle \ell \rangle = \frac{\partial}{\partial(\beta \Delta)} \ln Z_N^{\text{gen.}}(\beta E_0, \beta \Delta).$$

Approximating the partition function with Laplace's method (and computing critical points and checking stability), we find for the **gendered** system

$$\frac{\lambda_\mu^3}{V} e^{\beta E_0} = \frac{\langle j \rangle - \langle \ell \rangle (1 - e^{-\beta \Delta})}{(N - \langle j \rangle)^2}, \quad e^{\beta \Delta} = \langle \ell \rangle \frac{N - \langle \ell \rangle (1 - e^{-\beta \Delta})}{\langle j \rangle - \langle \ell \rangle (1 - e^{-\beta \Delta})}.$$

These equilibrium equations are identical in form to those for the **non-gendered** dimer system:

$$\frac{4\sqrt{2}\lambda_0^3}{V} e^{\beta E_0} = \frac{\langle k \rangle - \langle m \rangle (1 - e^{-\beta \Delta})}{(N - \langle k \rangle)^2}, \quad \frac{e^{\beta \Delta}}{2} = \langle m \rangle \frac{N - \langle m \rangle (1 - e^{-\beta \Delta})}{\langle k \rangle - \langle m \rangle (1 - e^{-\beta \Delta})}.$$

All of our previous qualitative results on Type I and Type II dimer systems, temperature conditions, and various phase behaviors transfer to the gendered dimer system.

All correct dimers in **non-gendered** and **gendered** system

Given the similarity between the non-gendered and the gendered dimer systems we can summarily state the conditions that must be satisfied for both systems to be in a state of all correct dimers.

Non-gendered dimer system

If the system is in a thermal equilibrium consisting entirely of correct dimers then T satisfies

$$k_B T < \frac{\Delta}{\ln(2N)}.$$

Gendered dimer system

If the system is in a thermal equilibrium consisting entirely of correct dimers then T satisfies

$$k_B T < \frac{\Delta}{\ln(N)}.$$

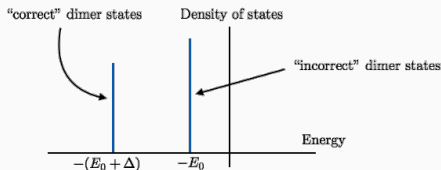
The above two are **necessary** rather than *sufficient* conditions for being in the equilibrium all correct dimers. In both cases, there is the same scaling with N .

Because the properties of the two systems are so similar, we can analyze one and make appropriate transformations to reach the other.

Extension #1: Distribution of correct binding energies

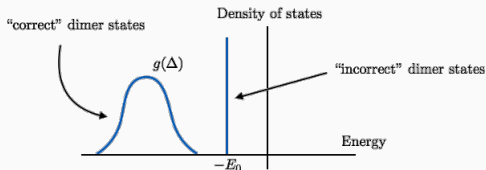
Distribution of energies for the dimer system

We have been working with a distribution of energies peaked at two values: $-E_0$ and $-(E_0 + \Delta)$.



A more general analysis would involve an interaction matrix or a distribution of energies for both correct and incorrect contacts.

However, this doesn't seem to lead to a soluble partition function, so we consider something simpler: a distribution of energies for **correct contacts** alone:



Partition function for distribution of correct contact energies

(Consider the non-gendered dimer system as an example) We have monomers α_k for $k = 1, \dots, N, N + 1, \dots, 2N$ which are distinct and exist as single copies. If two α monomers come into contact (say α_i and α_j where $i < j$) the two can form a dimer with binding energy

$$\mathcal{E}(\alpha_i, \alpha_j) = \begin{cases} -(E_0 + \Delta_i) & \text{if } j = i + N, \\ -E_0 & \text{otherwise.} \end{cases}$$

We note that $\mathcal{E}(\alpha_i, \alpha_j) = \mathcal{E}(\alpha_j, \alpha_i)$.

Computing the partition function for this system we find

$$Z_N(\beta E_0, \{\beta \Delta_k\}) = c_{0,N} \int_0^\infty dx dy \frac{e^{-x-y}}{\sqrt{xy}} \oint \frac{dz}{z} B_N(z) \prod_{\ell=1}^N [z x + \eta y (\delta_\ell - 1 + x)],$$

where $c_{0,N} = 1/2\sqrt{\pi}i\Gamma(N + 1/2)$,

$$\eta \equiv \frac{2\sqrt{2}\lambda_0^3}{V} e^{\beta E_0} \quad \text{and} \quad \delta_\ell = e^{\beta \Delta_\ell}.$$

and

$$B_N(z) = \frac{N+1}{2} \int_0^1 dt \left[\left(\sqrt{1-t} + \sqrt{t/z} \right)^{2N} + \left(\sqrt{1-t} - \sqrt{t/z} \right)^{2N} \right]. \quad (1)$$

Admittedly, this result appears intractable. But we can find equilibrium equations from this result.

Equilibrium for distribution of correct contact energies

From the previous partition function, we can derive the equilibrium conditions on \bar{x} , \bar{y} , \bar{z} .

$$\begin{aligned}1 &= N \int_{-\infty}^{\infty} d\Delta g(\Delta) \frac{\eta(e^{\beta\Delta} - 1 + \bar{x})}{\bar{z}\bar{x} + \eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})} \\N - \bar{x} &= N \int_{-\infty}^{\infty} d\Delta g(\Delta) \frac{\eta\bar{y}(e^{\beta\Delta} - 1)}{\bar{z}\bar{x} + \eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})} \\ \frac{1}{\bar{z}(\bar{z} + 1)} &= \int_{-\infty}^{\infty} d\Delta g(\Delta) \frac{\bar{x}}{\bar{z}\bar{x} + \eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})}\end{aligned}$$

These equilibrium conditions are associated with the order parameters $\langle \ell \rangle$ and $\langle m \rangle$ through the integral definitions.

$$\begin{aligned}\langle k \rangle &= \int_{-\infty}^{\infty} d\Delta g(\Delta) \frac{\eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})}{\bar{z}\bar{x} + \eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})} \\ \langle m \rangle &= \int_{-\infty}^{\infty} d\Delta g(\Delta) \frac{\eta\bar{y}e^{\beta\Delta}}{\bar{z}\bar{x} + \eta\bar{y}(e^{\beta\Delta} - 1 + \bar{x})}.\end{aligned}$$

Main Point? Not clear.

It's possible to write down the equilibrium conditions for this system, but it is not clear how to obtain physical properties from these conditions (or even if the effort is worth it).

Extension #2: Giving monomers and dimers structure

Rotation and vibration of dimers

We have previously considered monomers and dimers without any extended structure. But protein dimers have **rotational and vibrational energy**, and single monomers can have **rotational energy**.

Statistical mechanics review:

- **Rotational partition function:** For an object with moments of inertia A , B , and C , along principal axes, the rotational partition function is

$$\zeta_{\text{rot}} = \sqrt{\pi} \left(\frac{2\beta}{\hbar^2} \right)^{3/2} \frac{1}{(ABC)^{1/2}},$$

- **Vibrational partition function:** For a system with harmonic oscillator frequency ω the (quantum) partition function is

$$\zeta_{\text{vib}} = \frac{1}{2 \sinh(\beta \hbar \omega)}$$

To incorporate these effects, we will make the following assumptions:

- Correct dimers vibrate with frequency ω_{Δ} and incorrect dimers vibrate with frequency ω_{E_0} . Monomers do not vibrate at any frequency.
- All monomers have the principal moments of inertia A_0 , B_0 , and C_0
- All dimers have the principal moments of inertia A , B , C .

Rotation and vibration of dimers: new equilibrium conditions

To incorporate these effects, we will make the following assumptions:

- Correct dimers vibrate with frequency ω_Δ and incorrect dimers vibrate with frequency ω_{E_0} . Monomers do not vibrate at any frequency.
- All monomers have the principal moments of inertia A_0 , B_0 , and C_0
- All dimers have the principal moments of inertia A , B , C .

From these assumptions, we can derive the new equilibrium conditions

$$\frac{A_0 B_0 C_0}{\pi \sqrt{ABC}} \left(\frac{\hbar^2}{2\beta} \right)^3 \frac{2\sqrt{2}\lambda_0^3}{V} \frac{e^{\beta E_0}}{\sinh(\beta \hbar \omega_{E_0})} = \frac{\langle k \rangle - \langle m \rangle (1 - f^{-1})}{(N - \langle k \rangle)^2}$$

$$\frac{f}{2} = \langle m \rangle \frac{N - \langle m \rangle (1 - f^{-1})}{\langle k \rangle - \langle m \rangle (1 - f^{-1})},$$

where

$$f = \frac{e^{\beta \Delta}}{2} \frac{\sinh(\beta \hbar \omega_{E_0})}{\sinh(\beta \hbar \omega_\Delta)}$$

Main Point? New thermal effects.

Incorporating vibrational and rotational degrees of freedom lowers the effective binding energy for all species and consequently lowers the temperature at which system transitions to state where $\langle k \rangle \simeq \langle m \rangle \simeq N$.

Summary and ending thoughts

Summary and ending thoughts

1. **Non-gendered dimer system:** Able to find partition function, equilibrium conditions, numerically compute temperature dependence of order parameters, and transition temperatures
2. **Gendered dimer system:** Same as above.
3. **Extension #1–Spectrum of energies:** Able to find partition function and equilibrium conditions. Not clear how or whether to proceed.
4. **Extension #2–Physical molecules:** Able to find partition function (not shown in presentation) and equilibrium conditions. Makes system more physically plausible, but much more complicated.

Ending thoughts: Focus on simpler details first (without the energy spectrum or internal structure), to develop an understanding of the physical properties.

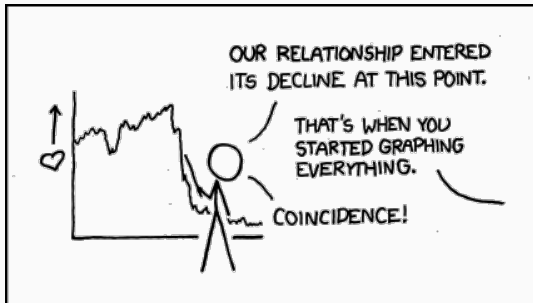


Figure 4: <https://xkcd.com/523/>

End