

# Embracing Entropy in the Design of New Materials

A common approach to designing a complex material is energy minimization. Like a ball in a cup, molecules at the microscale prefer to move into low-energy states. This logic can be used, for example, to design an assembly recipe for a material out of several different ingredients. In other cases, a material is designed to adapt at the molecular scale when it is strained or stimulated by e.g. light, heat, electricity, or breakage. Adaptations that we are currently able to build into a material include microscopic self-healing, stiffening, softening, shape change, light emission, opacity change, and colour change (among others). These are often designed to occur via an energy-minimising molecular pathway when the material is strained or stimulated. (Figure 1)

Elaborate materials can be designed, in principle, by this logic. But in practice, they often yield poor practical (experimental) success. The more complex the target structure, the more difficult it can be for the ingredients to follow the exquisite pathway leading to it. This is because the pathway is competing with “detours”: alternate routes leading to partial or incorrect structures. Detours may go energetically up-hill or down-hill,

and often lead to kinetically long-lived structures that are difficult to undo.

While each detour might be a rare event, the massive number of possible detours leading away from the correct pathway can easily reduce the success rate of the assembly or response. This is particularly true for elaborate pathways that involve different intermediate structures en route to the final structure. An analogy

is to imagine a tourist driving in a car to reach their destination without a map. The chance they take a wrong turn leading elsewhere is higher if there are more turns involved in the route, simply because there are more chances to go wrong.

## Entropy

The plethora of possibilities that molecules experience is called entropy. Mo-



molecular pathways must always contend with it. The goal of this article is to offer a suggestion (or a reminder) to find ways that we can embrace entropy, rather than fight it. Materials that have many paths of response or assembly to the final structure are more robust than those with just one or few 'designed paths'. We can thus use entropy to our benefit for making complex materials with remarkable functions.

Materials are always in motion at the molecular scale, due to thermal energy. This gives microscopic objects possibility, allowing them to visit different configurations, conformations, permutations, or orientations besides their energy-preferred ground state. Entropy at the molecular scale is a quantification of molecular possibility. Entropy drives building blocks towards structures that have more possibilities associated with them.

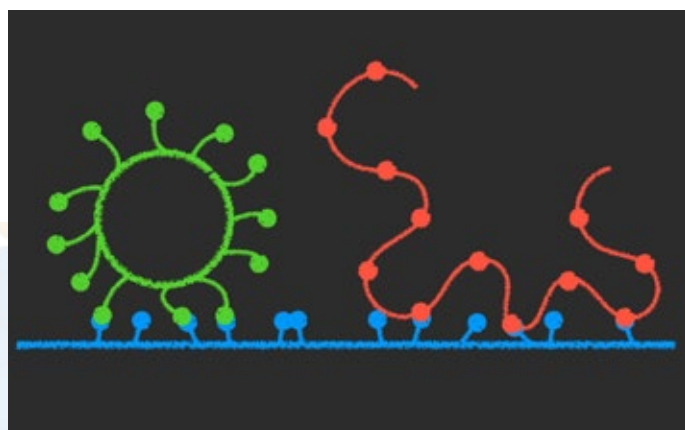
### 'Polymers with personality'

To date, a variety of designer polymeric materials actively utilize molecular motion to perform functions. Recent examples include materials that self-heal when damaged, dynamically adapt to strain using reversible crosslinks, or reshape and deform in response to light or local chemical environment. These might be called 'polymers with personality': materials with a molecular-scale reflex. These substances adapt and change their fate at the microscale, according to their external environment or a stimulus. Molecular design encodes the personality of the material that we see at the macroscale.

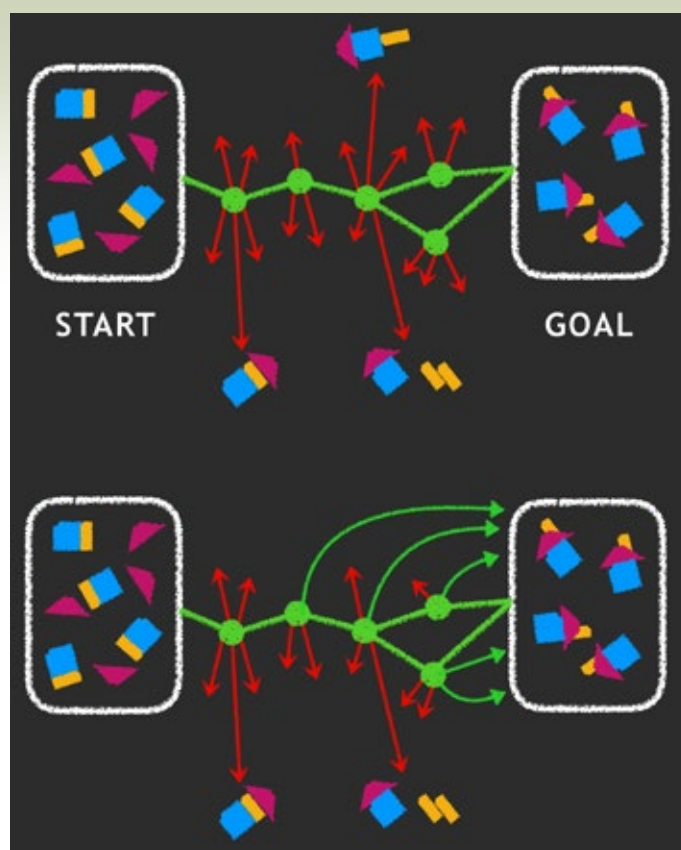
These materials are inspiring for their creative use of molecular entropy. But we can go further. As a molecular architect - theoretical or experimental - the next step is to understand how entropy is dictated by composition in a material, and how this changes when the material is altered.

### Inspiration from Life

Nature abounds with materials and systems where entropy is utilized for robust functionality. A practical instance for the design of polymeric materials is the way that interactions occur at cell surfaces. For example, T-cells in the human immune sys-



**Figure 2:** Multivalent nanoparticle (green) and polymer (red) interacting with a receptor-coated surface (blue). In both cases, the objects are interacting with the receptors via discrete binding groups (e.g. ligand, functional groups). The most significant multivalent entropy occurs when ligand-receptor bonds are weak, and when they can be independently bound or unbound



**Figure 1:** (Top) Initial ingredients evolve either spontaneously, or when simulated, to products via an assembly pathway (green) as shown schematically here. This pathway competes with a myriad of detours (red), leading to malformed structures and kinetic dead-ends. (Bottom) In a more robust molecular assembly or response process, there are more routes to reaching the target structure. Incorporating entropy into the design helps build more of these viable pathways, by taking advantage of molecular fluctuations around their energy-preferred states

tem interact with a target cell via many weak ligand-receptor bonds. This 'multivalent' binding paradigm causes the cell-cell adhesion to be extremely selective to the number of ligands and receptors on the T-cell and target cell. Binding is strong when the ligand-receptor density is above the threshold, yet extremely weak when below this threshold. (Figure 2)

Selectivity comes from the number of possible independent ligand-receptor bonds when the two cells are in contact. The relatively weak ligand-receptor bond strength permits the system to explore these binding permutations on a short timescale. This represents an entropy that contributes to the overall adhesion strength between the two cells. The entropy contribution varies, and thus can be tuned, with the number of ligands and receptors. This level of control is absent in energy-dominated 'monovalent' designs. Multivalency is a powerful yet generic microscopic paradigm that has already seen applications in synthetic molecular design, but much remains to be done.

In general, weak molecular interactions present the opportunity for entropic design. Weak bonds have the strong benefit of reversibility on short timescales, so that mistakes along an assembly or response pathway can be undone quickly. The



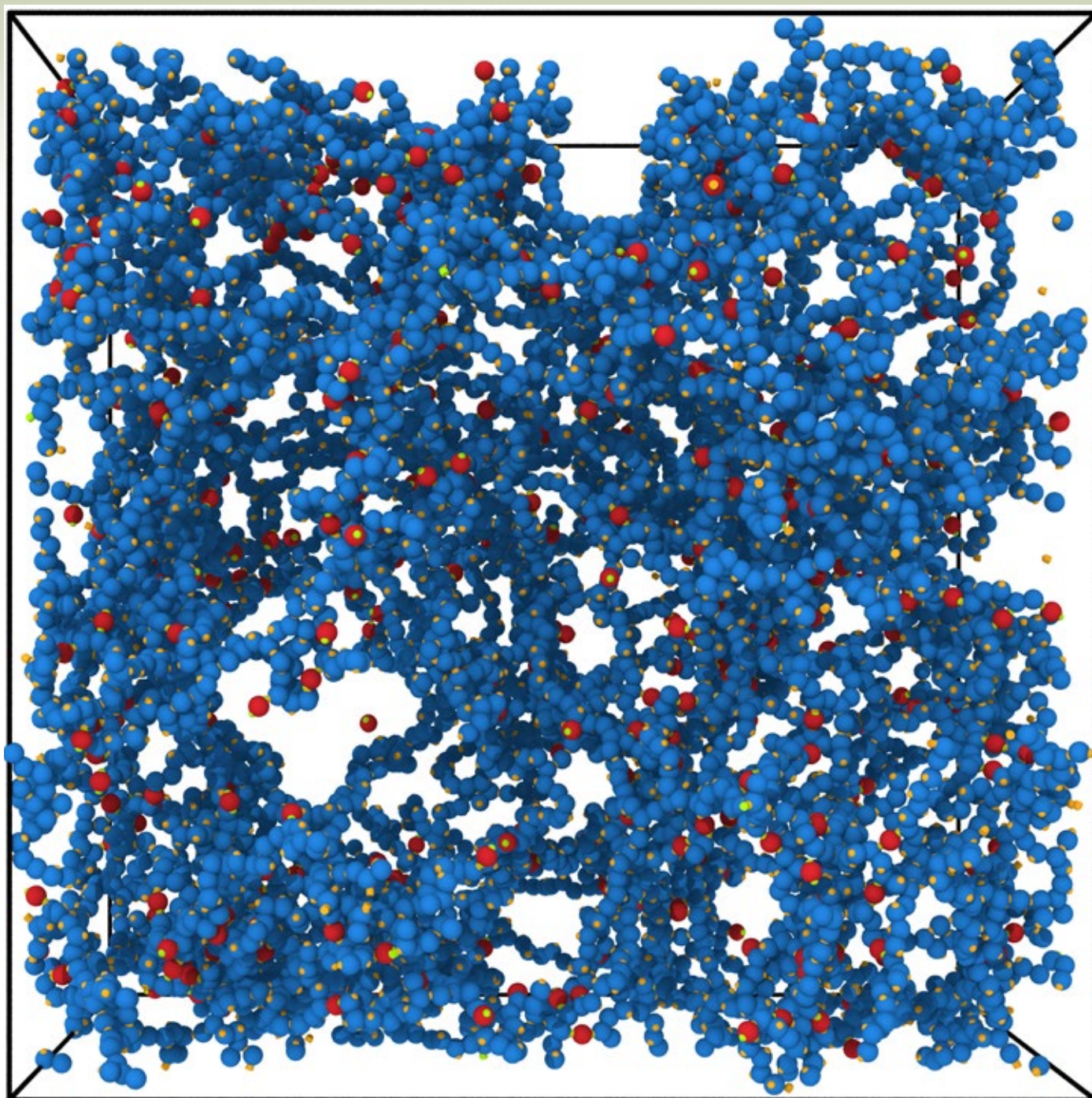


Figure 3. Molecular dynamics simulations are valuable tools for gaining microscopic insight into a material at equilibrium, and when deformed. Here, we are carrying out simulations of a polymer network (blue) with bonding units (yellow) on each monomer. Reversible crosslinks (red) can form one or two bonds with polymers using their own bonding units (green)

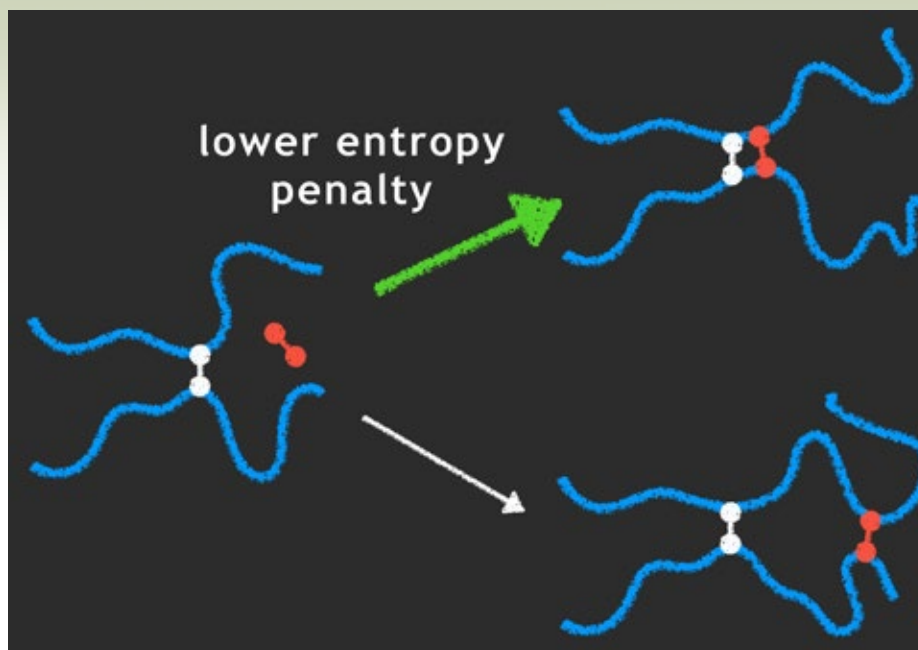
binding units can be designed to have specific interactions only with a subset of the molecular moieties in the system, yielding specificity. For example, two multivalent molecular entities will be strongly bound only when the majority of their different binding units are chemically complimentary. If not, the binding will be weak and reversible.

### Adaptive gels

For multivalent design, polymeric molecules are a promising candidate. But polymers themselves have nontrivial entropy. Polymers that are more confined, spatially restricted, or stretched have lower entropy than a free polymer. Manipulating the entropy of the polymers is thus another route to molecular design.

In current research with Wouter Ellenbroek and Cornelis Storm at Eindhoven University of Technology, I am studying a new material that exhibits this design. The material, a gel, is comprised of a permanently-crosslinked polymer network, along with reversibly crosslinking monomers diffusing within the gel. The reversible crosslinks allow the material to be strained to a much greater extent





**Figure 4:** Polymers (blue) attached to a permanent crosslink (white) in a polymer network, and a reversible crosslink molecule (red) in solution nearby. The entropy cost is lower when the reversible linker binds near the permanent crosslink (upper right), as the two adjacent polymers do not lose as much configurational freedom as when the reversible link binds further away (bottom right). The binding strength for the reversible crosslinks is the same in both cases. Thus, the linkers are entropically driven to recruit around the permanent crosslinks in the network. (Note that the four polymers extend beyond the cartoon shown, ultimately attached at their other ends to other permanent crosslinks in the system.)

than the native material without the reversible linkers, yet remarkably having the same native stiffness at small deformations. (Figure 3)

Through microscopic theory and modelling, we are finding that relatively weak-binding reversible crosslinks prefer to recruit around the permanent crosslinks. This is an entropy-driven phenomenon. (Figure 4)

Forming a reversible crosslink far from a permanent crosslink leads to greater spatial restrictions for the two polymer chains involved in the link. This leads to lower entropy. On the other hand, entropy loss is smaller when placing the reversible crosslink near a permanent crosslink, where the two polymers are already quite restricted.

By recruiting near permanent crosslinks during strain, the reversible linkers serve only to strengthen the former without altering the polymer network topology. This leads to the uniqueness of the material: it is far tougher, but with the same stiffness as the native gel without the reversible linkers.

### Vitrimers

Materials can also be designed to harness the intrinsic molecular entropy of the polymers themselves. A unique class of materials called 'vitrimers' provides an operational example. Vitrimers are polymer networks, containing polymer chains connected together by strong crosslink bonds. The material is strong and elastic at low temperature, yet can be reshaped at high temperature for self-repair and recycling.

This mechanism is based on an exchange principle that allows the crosslinks in the network to be exchanged, but not broken. As a result, the total number of crosslinks is constant; however, the exchanges give the material deformability that is comparable to that of molten glass: easily workable, deformable, and recyclable. Activation of the exchange mechanism is done by raising the temperature, which makes the analogy with molten glass a bit stronger. Various chemical realisation of this principle have been developed in recent years, for example the use of transesterification reactions to make ester crosslinks in networks dynamic.

### Swapping, not breaking

The ability of the material to be reshaped at high temperature relies on polymer entropy. All of the polymers are in motion in the liquid state, changing their conformations and exploring their local molecular neighbourhoods within the material. When new bonding partners are found, the network topology is changed. Energy minimization is negligible in these changes, as bonds are only swapping, and not breaking. Cooling from this entropic regime solidifies the network topology into place, bringing the system into a local energy minimum until heated again.

Using entropy in materials design requires microscopic insight, for which molecular theory and simulation are valuable assets. Active research in this area seeks to define clear links between microscopic design, and the unique - often unexpected - material responses that result. This research is alluring for industry and academia alike, due to the diversity of possible microscopic designs that can be harnessed for new applications or fundamental physical insight.

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**'Self-Consistent Field Lattice Model for Polymer Networks' door dr. Nicholas B. Tito, dr. W. Ellenbroek en prof.dr. Kees Storm (TU/e).**

[*Macromolecules*, 2017, 50 (24), pp 9788–9795]

Parts of this research have been performed within the framework of the 4TU. High-Tech Materials research programme 'New Horizons in designer materials' ([www.4tu.nl/htm](http://www.4tu.nl/htm)). The page for the project can be found here:

<https://www.4tu.nl/htm/en/new-horizons/reversible-crosslinking/>