There's plenty of room at the top

Channelling chemical intuition to conquer larger scales.

At its innermost core, nanotechnology is linked to the notion of control. One of the most iconic images in the history of nanotech is the 39 xenon atoms spelling 'IBM', which in 1990 amazed and inspired scientists and engineers[1]. It signalled the utmost level of control achievable in the materials world: the precise manipulation of single atoms— there was no more room at the bottom.

But going from spelling 'IBM' to building useful structures by controlling atoms one-by-one takes too much time. The issue of scalability has always been prominent in nanotech[2]. As a result, the top-down approach has dominated the scene, especially in the semiconductor industry — the main sector driving components miniaturization. Nowadays, transistors in commercial devices are steadily below 10 nm, with recent announcements to get down to 3 nm (ref. [3]). A few nanometres is approximately the size of a protein. It seems chemistry, which deals with objects typically not much smaller than 1 nm, could have easily gotten there. The bottom-up approach banks on the concept of self-assembly, where large supramolecular structures would build by themselves, directed by molecular recognition. This idea is very appealing because it relies on cheap and facile solution-based methodologies. Yet, although large-scale nanostructures have been demonstrated and surface patterning with a good degree of control shown — for example using block co-polymers[4] — even a tiny number of defects can fatally hamper the application of this technology in electronics.

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Perhaps the problem is that the bottom-up approach was initially thought to be in competition with the top-down approach, where in fact bottom-up can offer something different from the immediate needs of the semiconductor industry. Despite the challenges, we know that self-assembly systems can adapt and evolve according to environmental changes. They can process information, self-replicate, exist under out-of-equilibrium conditions and give rise to emerging properties. After all, we are the living proof of what self-assembly can achieve[5]. Taking inspiration from nature is going to provide much needed guidance. However, without the means to make assemblies with a similar level of precision our efforts are ill-fated and, frankly, they devalue the sensibility of chemists, their sense of beauty and drive for precision manufacturing.

But things are changing. Chemistry, synthetic chemistry in particular, is not an exact science in the same way that physics is. Its progress has hinged heavily on what chemists call chemical intuition. Even without a rigorous definition of basic concepts — such as resonance, and even the chemical bond — chemical intuition, rather than mathematical foundations, has been the engine behind progress in total synthesis, catalysis, polymer science and so on. However, it is now widely accepted that the golden era of covalent chemistry is behind us[6]. There are now sophisticated algorithms that can point chemists to the most efficient route to synthesize a compound[7]. The new frontier consists in channelling this chemical intuition to make molecules with controlled supramolecular interactions, and harnessing this knowledge to make hierarchical structures with atomic precision. From there, establishing a robust link between structure and function should follow suit. Easier said than done, surely! There are issues to be addressed everywhere: taming Brownian motion, working with weak, finicky interactions, developing a robust theoretical framework for out-of-equilibrium chemistry, coming up with suitable purification steps, inventing analytical tools for characterization and, as recently pointed out, devising multistep non-covalent syntheses[8]. It is likely that this approach will also support materials scientists working with soft matter — a synergy that could instil more rigorous control at the molecular level of their structures and systems.

Moving beyond covalent synthetic chemistry, parting ways from equilibrium chemistry and equilibrium supramolecular chemistry takes a lot of courage. It's going to be a pioneering effort, where everything needs to be figured out. It is almost like doing organic chemistry before nuclear magnetic resonance or the concept of chemical potential. But this is the great intellectual challenge awaiting chemists. For them, there is plenty of room at the top. ❒

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