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The nanotechnology of life-inspired systems

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For some decades now, nanotechnology has been touted as the 'next big thing' with potential impact comparable to the steam, electricity or Internet revolutions — but has it lived up to these expectations? While advances in top-down nanolithography, now reaching 10-nm resolution, have resulted in devices that are rapidly approaching mass production, attempts to produce nanoscale devices using bottom-up approaches have met with only limited success. We have been inundated with nanoparticles of almost any shape, material and composition, but their societal impact has been far from revolutionary, with growing concerns over their toxicity. Despite nebulous hopes that making hierarchical nanomaterials will lead to new, emergent properties, no breakthrough applications seem imminent. In this Perspective, we argue that the time is ripe to look beyond individual nano-objects and their static assemblies, and instead focus on systems comprising different types of 'nanoparts' interacting and/or communicating with one another to perform desired functions. Such systems are interesting for a variety of reasons: they can act autonomously without external electrical or optical connections, can be dynamic and reconfigurable, and can act as 'nanomachines' by directing the flow of mass, energy or information. In thinking how this systems nanoscience approach could be implemented to design useful — as opposed to toy-model — nanosystems, our choice of applications and our nanoengineering should be inspired by living matter.

Although we might not associate living cells with nanotechnology or engineering, they are intricate 'nanomachines' in which the key components (proteins, DNA, RNA) are nanometre-sized, structurally complex and information-rich entities that work in unison within various subcellular processes. To give one striking example: bacterial cell division occurs as a result of molecular recognition between several proteins (the Min proteins) working in combination with transport phenomena along concentration gradients. Together, these give rise to spatial oscillations (Fig. 1) that direct the division to occur at mid-cell with a precision of a few nanometres[1,2]. Importantly, this complex process occurs at exactly the right time, which is key to further exploration of systems nanoscience — namely, that living entities are capable of autonomously structuring matter at the nanometre scale by controlling reactions and self-organization not only in space (which nanotechnology has already largely mastered[3]) but also in time[2]. With such space–time control, dynamic patterns and structures arise (or emerge) from a seemingly unstructured clew of molecules. These molecules typically function within complex reaction networks that follow precisely tuned kinetics, and take place in dense and often compartmentalized intracellular environments whose role is to slow diffusion, resist homogenization, and allow for the maintenance of chemical gradients over relatively long times.

Design of life-inspired nanosystems

Let us first try to distil — and place in the context of nanotechnology — some key design blueprints that living systems use over and over again to build and operate their nanoscale machinery.

Molecular recognition. The process of molecular recognition, whereby different (macro)molecules engage complementary partners at short separations, is ubiquitous: DNA strands use hydrogen bonds to form double helices, and enzymes use different types of non-covalent interactions to bind their substrates, as do proteins forming multiprotein complexes. From its inception, nanotechnology has used similar approaches to synthesize extended nanostructures held together by van der Waals forces, hydrogen bonds, electrostatic forces or multivalent DNA binding, to name just a few[4]. The use of molecular recognition has proved very successful in controlling spatial organization of nanocomponents, culminating in the recent breakthroughs in DNA origami, which offers immense precision[3] and breadth of architectures[5] achievable with relatively simple design rules. However, molecular recognition alone can only assemble static, equilibrium structures: put plainly, it can make crystals but not cells.

Maintenance of non-equilibrium conditions. Perhaps the most distinctive design element of living systems is thermodynamic openness. Living systems are dynamic and require constant flows of matter or energy to power their reaction networks, maintain concentration gradients and enable active transport of molecules, for example along microtubules. Working under out-of-equilibrium conditions[6] is an established practice in chemical engineering, where many processes run in a continuous flow[7], but presents multiple design challenges at the nanoscale. How should artificial nanocomponents be used to interface chemical fuels and energy-degrading reactions to control their mode of organization? How can we move them around in controllable ways? How should we maintain their concentration gradients so as to direct systematic flows of other entities? In other words, the design challenge is to maintain nanosystems at steady-state conditions rather than at equilibrium.

Early non-biological examples of such systems include metastable nanoparticle assemblies held together only during light irradiation and disassembling when the external photon flux ceases[8], supramolecular assemblies acting as pumps driven by light[9], molecular suprastructures whose self-assembly and material properties are controlled by the consumption of chemical fuels[10], and various types of motile particles powered by catalytic surface reactions[11,12]. For the latter class of systems, theory predicts that

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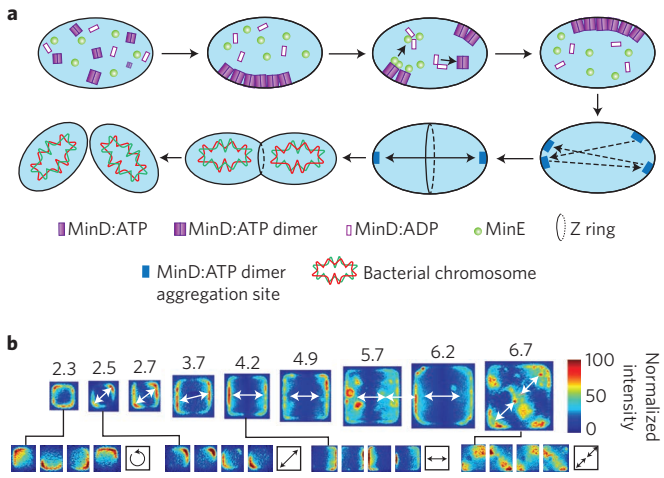

Figure 1 | Structure, function and external control of complex biological nanosystems. a, Oscillations of the Min system of proteins direct the formation of the Z ring and division of bacterial cells. Clockwise from upper left: initially, Min proteins are homogeneously distributed throughout the cell. Small, stochastic concentration variations lead to more MinD:ATP (shaded violet rectangles) binding and aggregating at a certain region of the membrane. After the aggregation site is nucleated, MinE (green circles) induces the hydrolysis of MinD-bound ATP to ADP, which causes the release of MinD from the membrane into the cytoplasm. MinD:ADP (open rectangles) is 'recharged' to MinD:ATP while diffusing through the cytoplasm. Since the original site is still consuming MinD:ATP, the concentration of MinD:ATP is highest at the farthest distance possible (approximately 'diagonal') from the original site, where the new aggregation event commences. The aggregate grows autocatalytically at this new aggregation site. The 'bouncing' of the aggregation site (bottom right) continues until the oscillation locks along the longest axis of the cell. In this stable oscillation cycle, the aggregation sites alternate between the poles of the cell. MinC (not shown) follows the movement of MinD and inhibits the formation of the 'Z ring' that defines the plane of cell division. Because the time-averaged concentration of MinC is lowest at the cell's centre, this is where the cell ultimately divides. The bacterial cell is shown as an oval (in reality it is rod-shaped) to simplify the illustration. **b**, The MinD oscillations can be spatially directed under imposed confinement. Here, the oscillation patterns are controlled by the sizes (given in micrometres) of square microwells in which the bacteria were cultured. Figure adapted with permission from: **a**, ref. 2, Wiley; **b**, ref. 44, Nature Publishing Group.

active particles themselves can create gradients along which they subsequently move, set up dynamic, phoretic interactions between themselves, and break symmetry to form various kinds of steady-state structures[13].

Feedback loops. Feedback is an essential control element and introduces the characteristic length scales of spatial pattern formation (as in skin stripes on fish or zebra) or the clocking timescales of temporal phenomena (as in circadian rhythms)[14]. It also controls auto-inhibition (negative feedback) and auto-amplification (positive feedback) processes that cells can use to maintain homeostasis[15], adapt or react to external cues[16], and provide the basis for self-replication[17]. In nanotechnology, we are only beginning to learn how to engineer feedback mechanisms and to interface them with various 'nanoparts'.

A recent example demonstrates a rational, bottom-up construction of an oscillating enzymatic reaction network controlled by small molecules (Fig. 2a)[18]. In a further example, organization of nanomaterials through coupled feedback loops coding for chemical oscillation reactions[19] was reported[20] (Fig. 2b). In this system[20], functionalized nanoparticles were coupled to a pH oscillator and exhibited both temporal cycling and propagation of waves of assembly and disassembly events. In another example, autocatalytic formation of peptide stacks competed with a negative mechanical feedback disrupting these assemblies, ultimately allowing self-replication of only certain types of nanostructures (Fig. 2c)[21,22]. In one final example, chemo-mechano-chemical feedback loops were built into a gel with micropillars that could be reversibly actuated between straight and bent forms (Fig. 2d)[23]. With a thermoresponsive gel and pillars containing a catalyst for an exothermic reaction, lowering the ambient temperature below a certain threshold causes the pillars to bend, which then triggers an exothermic reaction driving pillar unbending. This unbending, in turn, switches the reaction off, causing the temperature to fall again below the threshold, thus restarting the cycle. The net result is that the system acts as a homeostat, maintaining its local temperature in a narrow range dictated by the chemo-mechanical coupling.

Reaction–diffusion processes. Living cells are crowded media in which diffusion is slow. Although, at first glance, it might appear disadvantageous to rapid transmittal of chemical signals, slow diffusion is essential for a cell's proper functioning as it prevents homogenization and helps to maintain chemical gradients. When diffusion and other transport modalities, such as advection, couple with chemical reactions and/or self-assembly, the resulting reaction–diffusion processes can provide the means to control the flow of both matter and information at the nanometre and micrometre scales in processes such as chemotaxis, cell division, signalling cascades and oscillations, self-organization of the mitotic spindle and cell motility[2]. Translating these concepts into artificial nanosystems is still at a rudimentary stage, but some works have shown that it is possible to design systems that exhibit primitive forms of adaptability and signal processing in response to perturbations to coupled nonlinear chemical kinetics.

In a recent example, a family of wet, gel–gel stamping techniques was used to induce concentration gradients of complex reaction mixtures over arbitrarily shaped microdomains[24]. In particular, a chemical oscillator contained inside a gel can respond to different types of chemical 'foods' (methanol or formaldehyde) delivered to it[25]; the gel geometry amplifies the response and transmits food-dependent chemical waves to the surrounding environment (Fig. 3a). Another recent example is a system that mimics some key features of signalling cascades and is capable of rudimentary transfer and processing of chemical information[26,27]. In brief, a spatial pattern of trypsin enzyme is wet-stamped on a composite gel containing a trypsin inhibitor and trypsinogen, which can be autocatalytically converted to trypsin. A tug-of-war between trypsin inhibition and autocatalytic propagation front commences. When translated into a fluorescent readout, signals originating from densely packed or large features are amplified, whereas those from small or sparsely distributed features are effectively filtered out (Fig. 3b). Overall, this system uses a reaction–diffusion process to directionally pass, process and sharpen an image.

Compartmentalization and communication. Without specialized compartments, a cell would not be a 'nanofactory' supporting purposeful transfer of mass and information to desired locations, but rather a well-mixed reactor in which all components could potentially interact and react indiscriminately with one another. Making small reaction compartments such as vesicles, microdroplets, polymersomes (vesicles formed from block copolymers) or colloidosomes (colloidal particles self-assembled into hollow microcapsules) is nowadays well established, but the vast majority of these structures do not allow for the incorporation of out-of-equilibrium systems or processes, as they are neither sufficiently selective nor sufficiently open. The challenge is to build systems of

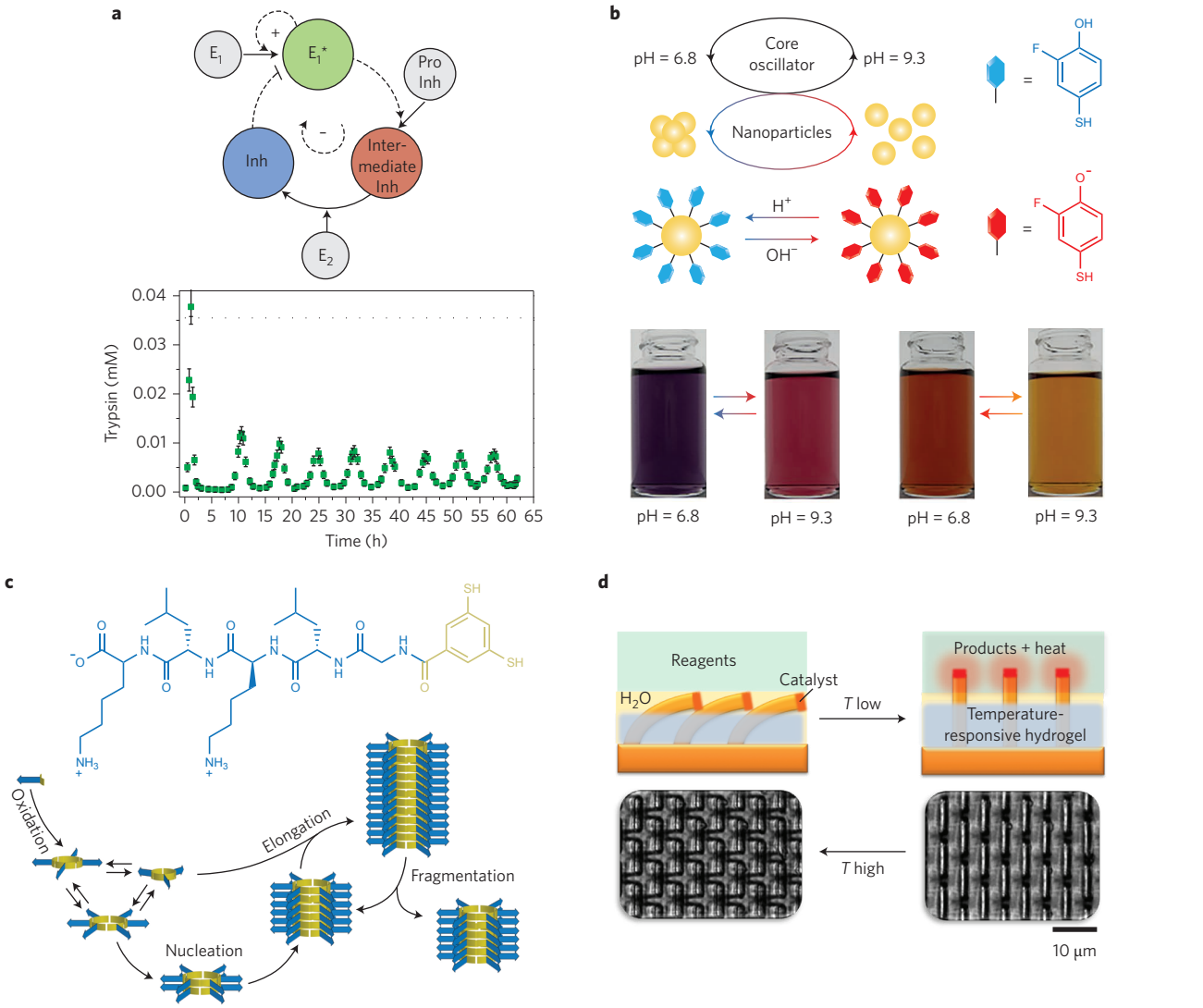

Figure 2 | Artificial nanosystems with built-in feedback. a, An enzymatic oscillator involving positive and negative feedback between enzymes (trypsin) and their substrates. Top: The wiring scheme. E_1, E_2, enzyme 1, enzyme 2; Inh, inhibitor; ProInh, pro-inhibitor. Bottom: Temporal oscillations in the concentration of trypsin. **b**, A chemical oscillator consisting of methylene glycol, sulfite and gluconolactone coupled to the assembly of nanoparticles. As the pH oscillates between pH 6.8 and 9.3, the 2-fluoro-*para*-mercaptophenol ligands on the nanoparticles become, respectively, protonated and deprotonated. These changes in the particles' surface charge translate into their rhythmic assembly and disassembly, as shown by colour changes of the solution (violet to red for gold nanoparticles, and orange to dark yellow for silver nanoparticles). **c**, Formation of disulfide linkages between aromatic dithiol headgroups of short peptides drives their assembly into cyclic aggregates that then stack to form 'nanopillars'. Mechanical vibration external to the system serves as a negative feedback that breaks stacks of a certain length more easily than others, effectively allowing the selection and self-replication of only one type of aggregate. For details see ref. 22. **d**, A homeostatic system in which catalysis on thermoresponsive micropillars (red region) causes changes in temperature (*T*), feeding back into mechanical deformations of the pillars. In effect, the system maintains approximately constant temperature. Figure adapted with permission from: **a**, ref. 18, Nature Publishing Group; **b**, ref. 20, Wiley; **c**, ref. 22, Nature Publishing Group; **d**, ref. 23, Nature Publishing Group.

dynamic compartments able to communicate between themselves and also with the outside world.

Chemical oscillating reactions can be confined to nanolitre droplets communicating with one another by the diffusion of one of the reagents[28,29]. Depending on reagent concentrations and/or system dimensions, droplet ensembles can exhibit coherent oscillations, antiphase oscillations or Turing patterns (Fig. 4a). Moreover, communication in nanoporous silica by a small-molecule-triggered mechanism has also been demonstrated (Fig. 4b)[30]. In this system, a chemical trigger opens the channels for one type of particle; the released cargo acts on a second type of particle, triggering a similar response. This is the first demonstration of an artificial signalling cascade between nanoscopic compartments. In possibly the most advanced artificial compartment yet built, a liposome harbouring an adenosine triphosphate (ATP) synthase and a bacteriorhodopsin is used to convert the energy of impinging visible light into a proton gradient that then drives the synthesis of ATP from adenosine diphosphate (ADP)[31]. This nanosystem is an excellent illustration of how the communication with an outside source of energy can couple with and maintain non-equilibrium conditions inside a rationally designed compartment.

How should we progress?

Although more examples of the design blueprints above could easily be given, the grand challenge is to integrate several or all of these features into functional nanosystems, for which both fundamental

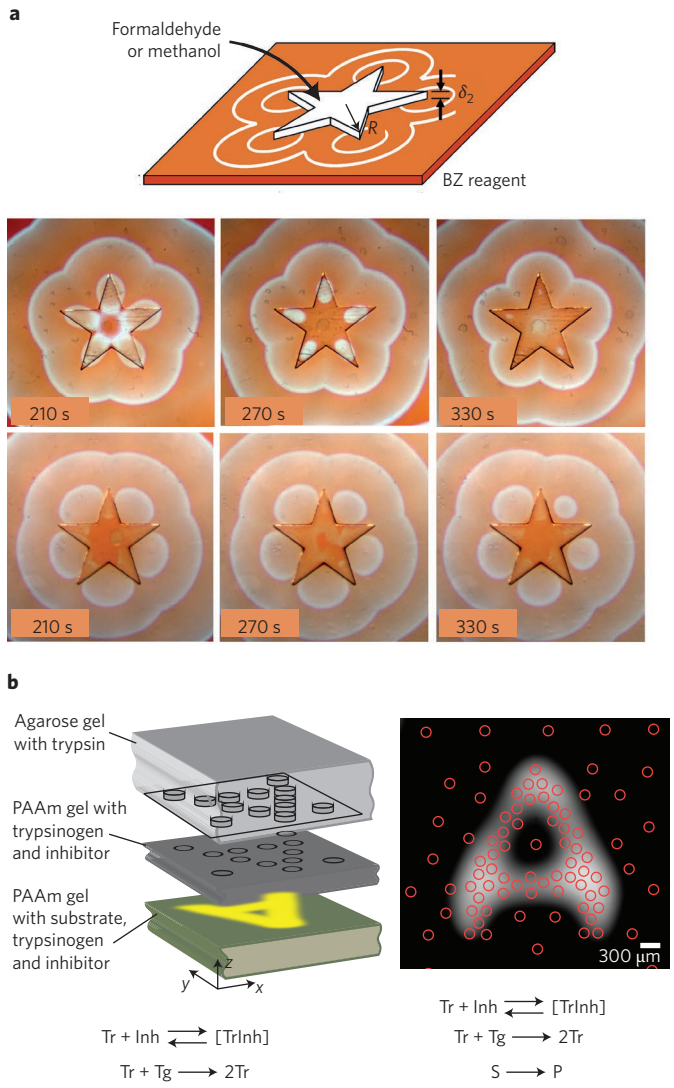

Figure 3 | Wet-stamped reaction–diffusion microsystems. **a**, Chemical 'food' (either formaldehyde or methanol) is delivered from a star-shaped agarose stamp into an agarose film soaked with the so-called Winfree formulation of the Belousov–Zhabotinski (BZ) oscillator. These 'foods' couple differently with the kinetics of the BZ oscillator and the geometry of the system; consequently, formaldehyde triggers chemical waves emanating from the star's tips (top row), whereas methanol triggers waves emanating from between the star's arms (bottom row). δ_2, thickness; *R*, radius. **b**, Recognition of the density of stamped microfeatures by a chemical reaction network. In addition to the fluorogenic substrate S, the target layer contains freely diffusing trypsinogen, Tg, and inhibitor, Inh. Autocatalytic production of trypsin, Tr, is due to the reaction of the incoming Tr with Tg. At the same time, Tr is inhibited by Inh. Depending on which of these competing reactions wins, the front of Tr can either propagate or be quenched. The first scenario occurs if the features in the stamp are proximal and 'reinforce' the local Tr influx; the second scenario occurs when features are distant. This principle is realized in the experiment illustrated in the right image where, out of the stamped features (red circles), only the clustered ones give rise to the fluorescent letter-A output signal in the target layer. PAAm, polyacrylamide; P, product. Figure adapted with permission from: **a**, ref. 25, APS; **b**, ref. 26, Wiley.

questions and practical ramifications can be envisaged. We would like to approach this challenge in a stepwise fashion.

Our first suggestion is to move beyond particles with only one type of ligand, because such particles can interact with their targets only in binary ways (bind/not bind) and cannot perform any additional functions. Instead, we envisage nanoparts presenting multiple surface chemistries: some interactions could be responsible for binding to desired targets, some could be switchable[32,33] to control the nature of interactions in time or in response to external triggers, some could be used to transduce chemical signals, and others could ensure proper solubility or biocompatibility. It would be desirable to have the ability to localize these components to discrete regions so that the interaction becomes directional. The chemistry to make multicomponent ligand shells is relatively well established[32–25], and there are early examples of how to localize different chemical functionalities to different locations, for example by means of the underlying local curvature[36].

Next, we should learn how to interface these multicomponent nanoparts with existing biological systems. In one recent and illustrative demonstration[37], multifunctional nanoparticles, after their uptake by cancer cells and upon an appropriate trigger, were able to convert a prodrug into a cancer drug that then was converted by an enzymatic cascade into a cytotoxic compound (Fig. 5a). In effect, the nanoparticles controlled a system of enzymatic reactions. We emphasize that the general (and elegant) concept of multifunctional nanoparticles controlling (bio)systems can offer distinct advantages over classical organic synthesis. Incorporating catalytic activity, proper solubility and switchability all into a single molecule would be a daunting proposition, whereas making nanoparticles combining all these functions would require adsorbing on the particles relatively simple organic ligands — each possessing one function — in desired proportions.

Another form of (bio)systems control might capitalize on the size of nano-objects. Could nanoparts with sizes commensurate with those of biomolecules replace the (perhaps malfunctioning) biological components within larger structures (for example multiprotein complexes)? Could nanoparticles presenting charged and hydrogen-bonding groups[35] be used to replace some subunits of a ribosome known to be held together by such interactions? How would the ribosome's function be modulated by such a replacement? These and similar questions can now be studied by chemists and nanotechnologists, because many protein complexes — including ribosomes stabilized by covalent links[38] — have been reconstituted *ex vivo*.

Outside the biological domain, we see much potential for 'active' nanoparts in controlling chemical processes and reaction networks. Metal nanoparticles covered with photoswitchable ligands and exposed to ultraviolet or visible light can be toggled between catalytically inactive (when aggregated) and catalytically active (when dispersed) states (Fig. 5b)[39]. With a wide variety of photoswitchable molecules responsive to different wavelengths of light available, one could start constructing systems of multiple particles harbouring different catalysts. The selective assembly/disassembly of these components by light of different wavelengths could then dictate the sequences in which organic reactions are catalysed. Depending on which catalysts are activated at what times, one could synthesize different products from the same initial pool of substrates. In the example in Fig. 5c, the simplest network, based on two types of nanoparticulate catalyst, could make either an intermediate, **4**, in the synthesis of blood coagulation factor VII antagonist, **A** (Ajinmoto), or an intermediate, **5**, in the synthesis of a urotensin-II receptor antagonist, **B**.

Ultimately, nanoscale controls and entire interaction networks could be embedded within containers (nano- to micrometre scale), thus allowing these systems to function independently from their environment. One popular motivation to study such constructs is in the context of building cell mimics. While this direction is interesting in the context of origins-of-life research, we do not see such protocells[40,41] becoming as useful as real cells, which synthetic biologists can nowadays program almost at will to achieve various

biosynthetic functions. Instead, we see systems within nanocontainers as potential chemical factories performing syntheses that would otherwise be hard to accomplish or that require harsh chemical environments. Interestingly, recent work indicates that increasing the curvature of the confining compartment can shift chemical equilibria[42]. Results such as this are significant because they point to the possibility of rationally modifying reaction thermodynamics by confinement at scales larger than molecular. Furthermore, carrying out reactions in small containers offers an alternative route to screening large numbers of suitable reaction conditions for finding interesting behaviour in reaction networks[43]. Yet there is at least one technical obstacle in realizing the synthetic potential of confined nanosystems — they need to be able to communicate with the environment. Imposed geometry can be one form of direct control, as has been shown for Min oscillations that can adapt to and be controlled by the dimensions and shape of bacteria confined to microscopic wells (Fig. 1b)[44]. However, geometrical constraints alone do not open the system up to selective mass uptake, energy transfer and product removal. The key is to maintain such reactors in steady states. And this requires pumps able to move matter against a concentration gradient. Currently, no non-biological nanopumps exist that are capable of performing such tasks across physical boundaries (membranes). Designing them should therefore be high on our wish list. We speculate that ratcheting phenomena that rectify Brownian motions by imposing asymmetric potentials[45] could be a useful approach.

Naturally, there are many more directions that could be explored and more general (or even visionary) questions to be asked. For one, it is certainly exciting to think about self-replicating nanosystems[46] although it is not yet clear to us what their practical uses might be. There is also much room for exploring the role of feedback in controlling the fidelity of systems assembly and operation. It is well known in biology[47,48] that feedback loops can help to minimize error rates during protein and DNA synthesis, and can aid recognition of correct substrates during their binding to surface receptors. Could we use similar 'wiring schemes' to construct nanosystems that correct for errors or defects? Ultimately, once the construction of individual nanosystems is mastered, it would be interesting to study their ensembles — and watch closely at what point the parts we put in start functioning in ways we might not anticipate or even understand.

We expect that in time, nanosystems designs will be integrated into the myriad of 'smart' or 'intelligent' materials that have been reported in the past decade, and that often are not particularly smart or intelligent. Instead of responding to a single trigger (change in temperature, pH, salt concentration) in a rather linear fashion, materials incorporating nanosystems should be able to sense multiple parameters and use internal computational algorithms to decide on the most appropriate response, which they could amplify through in-built nonlinearities. They could also ultimately be interfaced with living systems, for example as components in biocompatible electronics[49] or optofluidics[50].

No doubt there will be many roadblocks on the way. At the level of instrumentation, time-resolved modalities (flow transmission electron microscopy or ultrafast spectroscopies) will be needed to monitor processes in nanosystems, which are inherently dynamic. On the conceptual level, the architecture and dynamics of any non-trivial systems with feedback and other in-built nonlinearities cannot simply be guessed; modelling is essential. Consequently, there is urgent need for software in which the user can define a system's parts and then study their behaviour under different wiring schemes. To be used by experimentalists, such software should be general in scope and easy to use, calling for the development of something such as a NanoCAD for nanosystems (Fig. 6). Other theoretical tools, not widely used in the nanotechnology community at present, should include stability analysis and phase-space

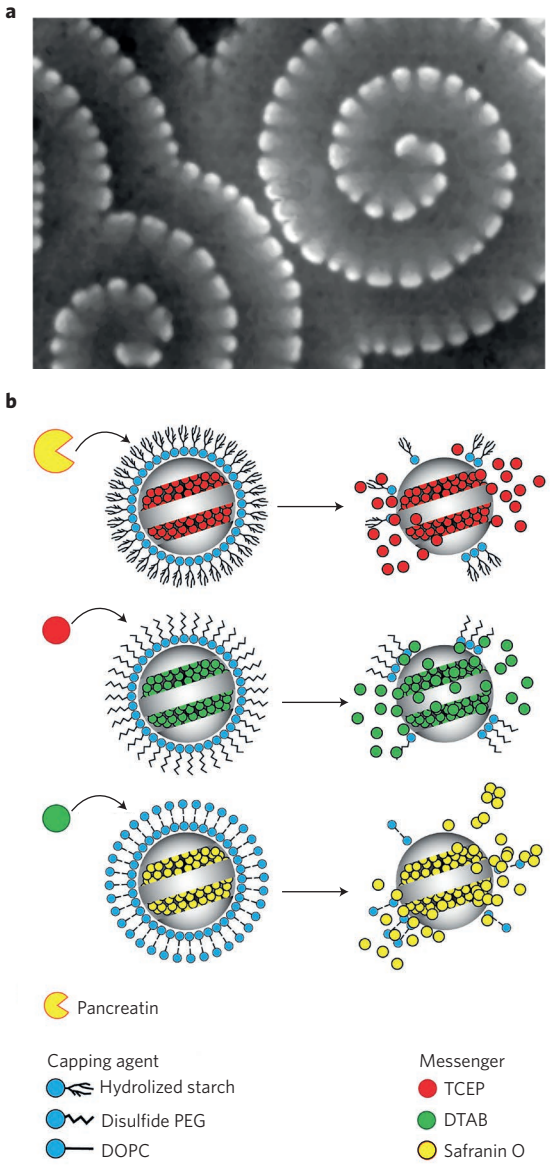

Figure 4 | Communication between nanosystems. a, Chemical spiral waves propagating between aqueous nanodroplets supporting BZ oscillations and suspended in an oil phase. Communication between the droplets is mediated by the diffusion of some reaction intermediates (Br_2 or BrO_2). Area shown 3.72 × 4.82 mm^2. **b**, Illustration of system of mesoporous nanoparticles relaying chemical information. The cargo (red) released by pancreatin from the first type of particle opens the pores of a second type of particle, which, in turn, release their cargo (green) to open the pores of the third type of particle to deliver the final load (yellow balls). The numerous molecules used to construct this system (sugar derivatives, disulfide polyethylene glycol (PEG), messenger small molecules, safranin indicator) are described in detail in ref. 30. DOPC, 1,2-dioleoyl-*sn*-glycero-3-phosphocholine; DTAB, dodecyltrimethylammonium bromide; TCEP, tris(2-carboxyethyl)phosphine. Figure adapted with permission from: **a**, ref. 29, NAS; **b**, ref. 30, Wiley.

dynamics[6] as well as stochastic modelling to describe systems with statistically small numbers of nanocomponents[43]. Realistically, this effort will require close collaboration between experimentalists and theorists, always an enriching (if challenging) enterprise.

Notwithstanding these potential complications, we are optimistic that such capabilities will be developed in the near future. We

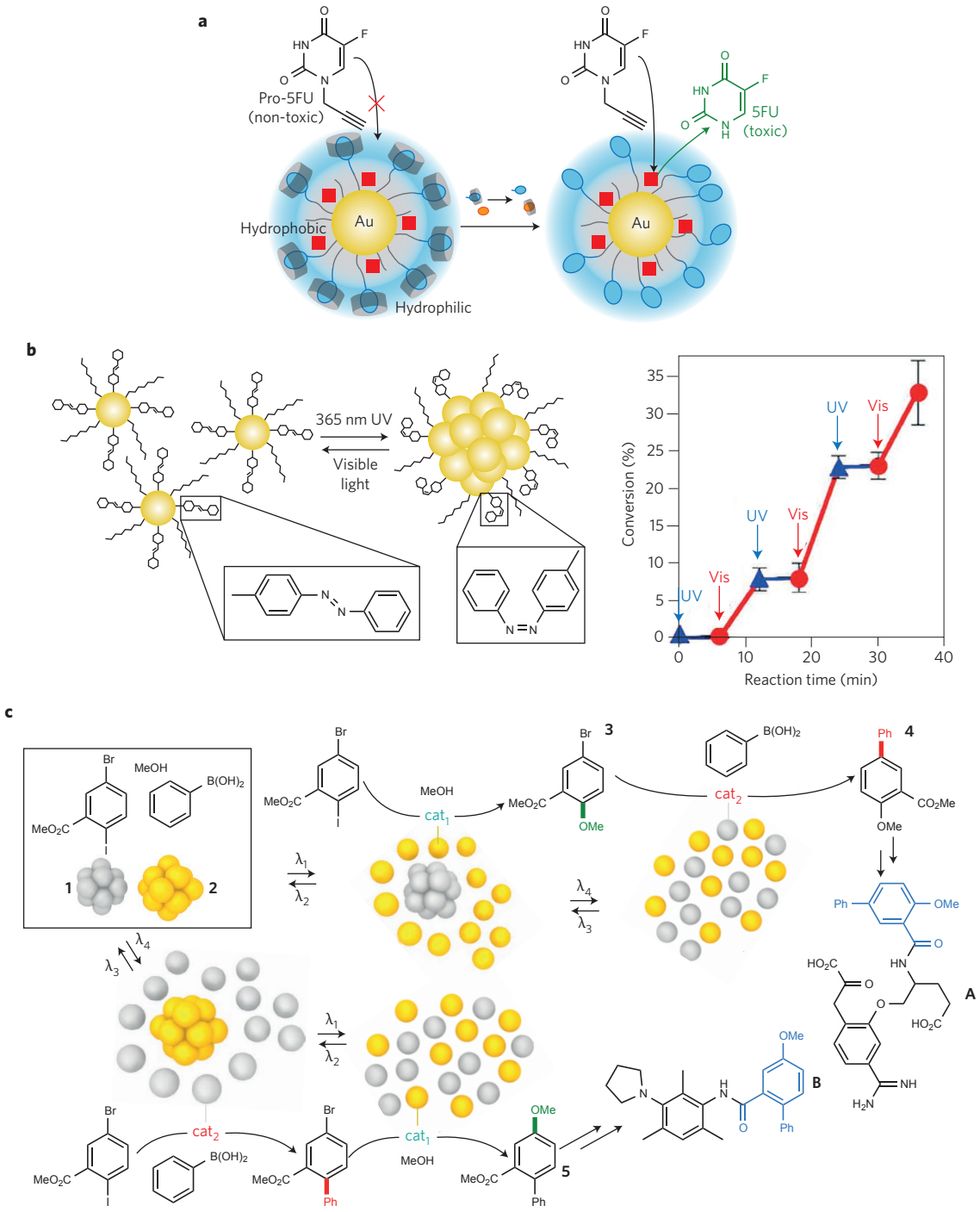

Figure 5 | Nanoparts for existing and hypothetical nanosystems. a, Gated nanoparticles that can be activated on demand to control biochemical reactions inside living cells. On displacement of cucurbit[7]uril 'gate keepers' (grey disks in the left panel), the prodrug can reach catalytic centres (red squares) and be converted to 5FU (5-fluorouracil), which is ultimately toxic to cancerous cells. **b**, Gold nanoparticles covered with a mixed monolayer of dodecylamine surfactant and photoswitchable azobenzene-terminated ligands can be aggregated on ultraviolet exposure and redispersed on irradiation with visible light. Importantly, dispersed nanoparticles are catalytically active in hydrosilylation of 4-methoxybenzaldehyde; aggregated nanoparticles are catalytically inactive. The plot on the right shows the percentage conversion for the hydrosilylation reaction catalysed by the gold nanoparticles. The reaction is switched 'on' by visible light (Vis; red portions of the curve) and 'off' by ultraviolet (UV; blue portions). **c**, Suggested extension of **b** to a system in which two types of photoactivated nanoparticle control sequences of catalytic reactions leading to different products. One type of nanoparticle (yellow) harbours a glycine- or phenanthroline-based catalyst (cat_1) and molecular switches responsive to wavelengths λ_1 and λ_2. The other type of nanoparticle (grey) harbours a palladium-based catalyst (cat_2) and molecular switches responsive to wavelengths λ_3 and λ_4. The initial dispersion of the yellow nanoparticles and activation of glycine-based catalyst will result in the Ullmann-type reaction, and subsequent activation of the palladium-based catalyst will yield methyl-2-methoxy-5-phenylbenzoate **4** (via Suzuki coupling). When, however, the two nanoparticles and catalysts are light-activated in the reverse order, **1** and **2** will first undergo a Suzuki coupling, and the products of this reaction will then give methyl-5-methoxy-2-phenylbenzoate, **5**. Figure adapted with permission from: **a**, ref. 37, Nature Publishing Group; **b**, ref. 39, American Chemical Society.

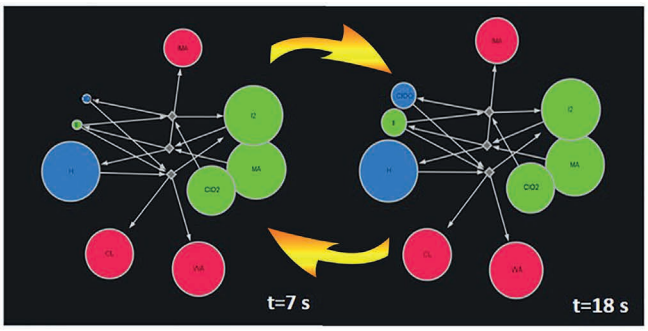

Figure 6 | Visualizing systems by 'etch-a-system'. Dynamics of even very complex systems with multiple feedback loops and arbitrary interaction kinetics can be modelled and visualized by the 'etch-a-system' Kinematicon software created in the Grzybowski group. Shown here is the network of interactions underlying the so-called CDIMA chemical oscillator. Circular nodes correspond to the participating chemicals/intermediates, and the smaller, diamond-shaped nodes correspond to reaction operations. Once the network is drawn and the simulation commences, the sizes of the nodes change proportionally to concentration variations over time. Here, the two nodes closest to the arrowhead of the top curved arrow exhibit rhythmic concentration changes (that is, oscillations).

see it as a necessity (and an exciting one) to move from assembling static nanostructures to synthesizing bioinspired, dynamic nanosystems. Without adopting a systems approach, nanotechnology risks becoming an obsolete art of making intricate particles with little practical impact. The systems approach offers unprecedented means of programming and controlling multiple processes simultaneously, much like in living systems, whose complexity we would ultimately like to understand and emulate.

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