A nature-inspired approach to reactor and catalysis engineering

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Mechanisms used by biology to solve fundamental problems, such as those related to scalability, efficiency and robustness could guide the design of innovative solutions to similar challenges in chemical engineering. Complementing progress in bioinspired chemistry and materials science, we identify three methodologies as the backbone of nature-inspired reactor and catalysis engineering. First, biology often uses hierarchical networks to bridge scales and facilitate transport, leading to broadly scalable solutions that are robust, highly efficient, or both. Second, nano-confinement with carefully balanced forces at multiple scales creates structured environments with superior catalytic performance. Finally, nature employs dynamics to form synergistic and adaptable organizations from simple components. While common in nature, such mechanisms are only sporadically applied technologically in a purposeful manner. Nature-inspired chemical engineering shows great potential to innovate reactor and catalysis engineering, when using a fundamentally rooted approach, adapted to the specific context of chemical engineering processes, rather than mimicry.

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Introduction

Nature-inspired engineering researches the fundamental mechanism underlying a desired property or function in nature, most often in biology, and applies this mechanism in a technological context. In the context of chemical engineering, we call this approach: *nature-inspired chemical engineering* (NICE) [1].

Application of biological mechanisms to a non-physiological context in reaction engineering requires adaptations, because the relevant time scales and available building blocks are different. Also, we are able to manipulate parameters such as temperature and pressure, which are much less tunable in biology. Hence, like in an abstract portrait, essential aspects of the subject are preserved, but not literally, emphasizing those features that serve a desired purpose. Such features underpin the rational design of an artificial structure that uses the same fundamental mechanism as the natural system. The ultimate implementation is assisted by theory and experimentation. NICE aims to innovate, guided by nature, but it does not mimic nature, and should be applied in the right context.

Emphasizing reactor and catalysis engineering, we illustrate how mechanisms used in biology to satisfy complicated requirements, essential to life, are adapted to guide innovative solutions to similar challenges in chemical engineering. These mechanisms include: (1) use of optimized, *hierarchical networks* to bridge scales, minimize transport limitations, and realize efficient, scalable solutions; (2) careful *balancing of forces* at one or more scales to achieve superior performance, for example, in terms of yield and selectivity; (3) emergence of complex functions from simple components, using *dynamics as an organizing mechanism*. Figure 1 presents an overview.

In this way, NICE complements an ongoing revolution in bioinspired chemistry and materials science [2**,3**,4–6], which already sees applications in, for example, enzyme-mimics and antibody-mimics for catalysis [7–10] and in artificial photosynthesis [11•,12•,13–15]. These applications implement essential mechanistic steps of the biological model system at molecular and supramolecular scales. Hierarchically structured bionanocomposites have superior properties by synergy, unmatched by their individual components, inspiring novel material designs.
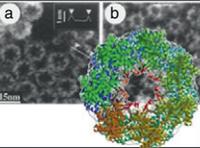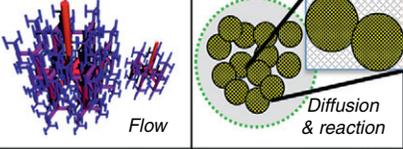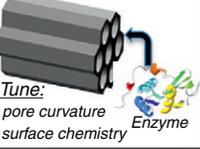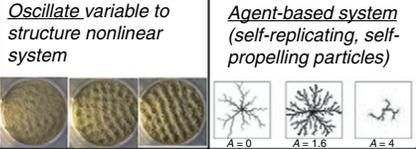
As we now illustrate, nature has more to offer to reaction engineering when considering larger length scales and the time domain. In addition, the manipulation of force balances as an organizing mechanism merges bioinspired chemistry, chemical and materials engineering.

Hierarchical transport networks

Transport is crucial to living systems, and to reaction engineering alike. Trees and mammalian physiological networks share common architectural traits that endow them with vital properties. The vascular and respiratory networks have a branched, hierarchical architecture that is *fractal* between macroscopic and mesoscopic length scales, having features that look similar under repeated magnification [16**,17]. At those scales, *convective flow* is the dominating transport mechanism and the channel walls are impermeable. On the contrary, channels are

2 Reaction engineering and catalysis

Figure 1

Overview of nature-inspired chemical engineering, as applied to catalysis and reactor engineering, from observation to concept, design and realization. The bottom row indicates the stage of development, from green (ready for industrial development) to red (early-stage). All images personal, and from [21**,23*,46*,57*,81,92,95*,102], except on top row: lung [103]; leaf [104]; GroEL heptamers [53]; bacterial colony on Petri dish [105].

almost *uniformly sized* at mesoscopic to microscopic length scales, approaching those of individual cells. In capillaries or in the acini of the lung, exchange occurs via the cell walls, and *diffusion* is the principle transport mechanism. This is most efficient, costing no metabolic energy [18*]. Indeed, the transition between biological circulatory networks and networks of exchanging channels frequently corresponds to a Péclet number around 1. Furthermore, as discussed below, such architectures are optimal in several other ways that would benefit chemical engineering applications.

The fractal architecture of the upper respiratory tract, the arterial network and tree crowns connects multiple microscopic elements to a single macroscopic feeding/collection point (trachea, heart, stem). This occurs via equal hydraulic path lengths that provide equal transport rates to and from the cells. Cell size is remarkably constant across species, despite considerable differences in size between organisms. Feeding more cells occurs via trees with a larger number of branching generations. The fractal geometry of biological transport networks facilitates scale-up, by preserving cell access and function irrespective of size. Achieving uniform access and macroscopically homogeneous operation are chemical engineering challenges as well. This insight has led to the construction of fractal distributors and injectors for multiphase separation, mixing and reaction processes [19,20*,21**].

Figure 2 includes an example of a two-dimensional ($D = 2$) fractal distributor from our laboratory, produced

Figure 2
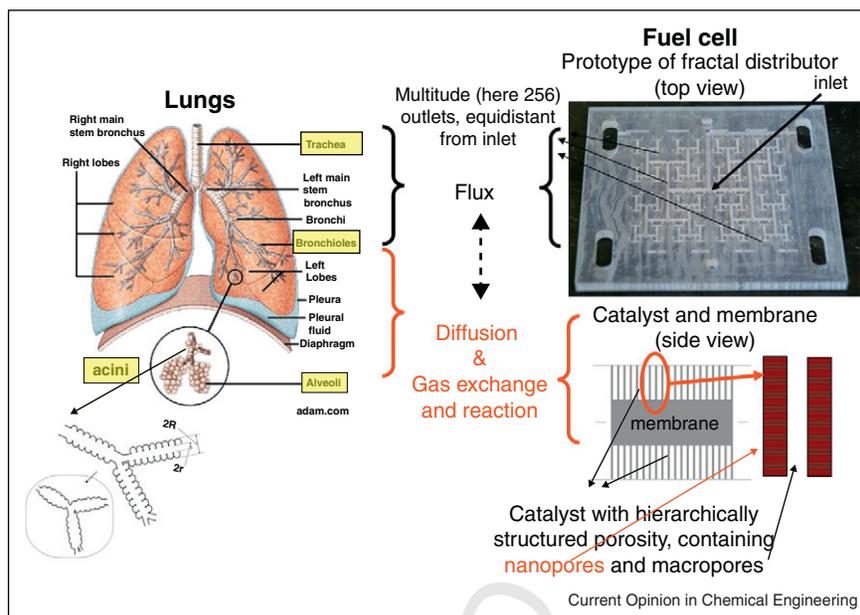
Fuel cell design guided by the architecture of the lung, and the associated physical mechanisms.

by stereolithography, for a PEM fuel cell design inspired by the structure of the lung. Fluid entering the distributor through a single inlet flows through the branching channels, and ultimately leaves the distributor through a square array of outlets, which are hydraulically equidistant from the inlet. Thus, the space under the distributor is accessed uniformly. This fractal distributor could uniformly feed air over the catalytic layer of a PEM fuel cell, as well as collect water, circumventing non-uniformity issues of serpentine and other channel geometries [22]. Such structures could also homogeneously feed high-throughput setups, or uniformly heat or cool surfaces. They could be integrated into microfluidic devices; already common in multi-channel microreactors is a binary tree, based on n times repeated Y-branching, to serve a one-dimensional array of 2^n channels ($D = 1$).

In nature, the fractal dimension, D, depends on the transport network. The respiratory network of a lung fills space, hence $D = 3$. In other cases, as for botanical trees, the structure fills less than three-dimensional space, but is more than area-filling, therefore $2 < D < 3$. For example, splitting all branch tips of a self-similar tree into 6 new branches that are half as extended leads to a tree with $D = \log 6/\log 2 \approx 2.6$. Such is the case for the fractal injector shown in Figure 3 [21••,23•].

Figure 3
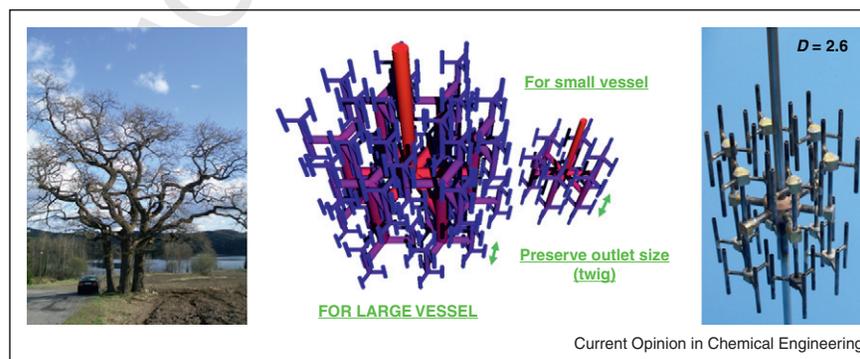
Fractal injector for multiphase reactors, guided by the scaling architecture of tree crowns.

Submerged in a fluidized bed, this fractal injector uniformly distributes gas throughout the reactor. Maintaining at least minimum fluidization via a bottom distributor plate, extra gas injected via the fractal injector, directly into the emulsion phase, promotes micromixing around the branch tips. This increases mass and heat transfer, and improves gas–solid contact, because of kinetically delayed bubble formation. For multiphase reactors, the complex hydrodynamics are a major hurdle in scale-up [24]. A fractal injector facilitates scale-up: like in a lung or tree, the sizes of the outlets and the distances between outlets are maintained in larger reactors, by increasing the number of branching generations. The optimal distribution of outlets and value of D depend on mixing characteristics and reaction times [21••]. Utilizing a fractal injector can bring the overall reactor behavior closer to plug flow, which is often advantageous to increase conversions and, depending on the kinetics of the competing reactions, selectivity [23•]. For applications at high temperatures and large scales, the hierarchical structure lends itself well to modular, metallic construction.

Another remarkable feature of many scaling, anatomical trees is that they are near optimal from the point of view of flow resistance, thermodynamics, and robustness over time and over a range of operating conditions. Often, this is tied to the particular geometric progression of branch lengths and radii, and the minimum length scale of the scaling regime. Such observations date back almost a century, when Murray showed that, for the vascular network, mechanical resistance and the cost of maintenance of blood in the body are minimal thanks to a branched structure in which the sum of the cubes of the diameters of daughter branches is equal to the cube of the diameter of the parent branch [25,26]. West *et al.* [27•,28,29] further postulated that space-filling, biological circulatory networks relate to mechanical and thermodynamic optimality, and are the cause behind Kleiber's allometric scaling law (energy dissipation proportional to body mass to the power). Bejan and co-workers [30••,31] introduced a thermodynamic theory to derive optimal architectures satisfying various criteria, for example, maintaining uniformity, reducing flow resistance [32] or minimizing the maximum temperature of a surface. Using this 'constructal theory' remarkable parallels between trees in nature and engineering were found. Frequently, optimality corresponds to architectures that realize equipartition of entropy production, as was discovered for the lung [33]. Tondeur and Luo [34,35] applied constructal theory to distributors that compromise costs related to pressure drop, viscous dissipation, and hold-up volume.

When diffusion is the dominating transport mechanism, the architecture of biological transport networks changes from fractal, scaling, to uniform, non-scaling, in particular when exchange processes via the walls occur, as in acini

and leaves. Translation to catalysis engineering requires care, as objectives and constraints might differ. For example, reactor-engineering requirements often determine minimum catalyst particle size, resulting in possible diffusion limitations. Other criteria are problem dependent: minimizing costly catalytic component to achieve a certain yield, maximizing conversion, mitigating effects of deactivation, achieving a particular product distribution, and so on. We do not review this subject in depth here, but refer to Ref. [36]. Simulation relies on a range of modeling approaches [37], which are increasingly multiscale [38,39]. Recent possibilities to control pore network properties at multiple length scales via new synthesis methods [40,41,42•] should be accompanied by theoretical optimization. If the intrinsic catalytic activity per unit nanoporous catalyst is kept constant, as in zeolites or catalytic clusters supported on a mesoporous carrier, then virtually no benefit is gained from a broad macro/mesopore size distribution to increase activity [43,44•], increase stability [45,46•] or control selectivity [47]: optimal porosity and optimal average macro/mesopore size are the main parameters. Other criteria may lead to different optima [48,49]. Most important is that the hierarchically structured catalyst consists of nanoporous domains or grains without local diffusion limitations, interspersed by larger pore channels of optimized size. Again, this matches physiology: cells of the same type are of the same size, and interspersed by capillaries of more or less uniform size that transport nutrients and remove waste products by diffusion.

The ability to bridge scales and efficiently couple transport and reaction processes by nature-inspired design promotes process intensification [50]. This is illustrated by Figure 2, showing how the structure of the lung inspires the design of a PEM fuel cell, with the aim to drastically reduce the required amount of expensive Pt catalyst to achieve a desired power density, facilitate water management, maintain uniform operation, increase robustness, and facilitate scale-up.

Force balancing

From the DNA double helix to virus capsids, biology is replete with supramolecular assemblies that self-organize from molecular and ionic components via balanced, non-covalent interactions [3,51]. Hierarchically structured materials can be synthesized using biological templating or mechanisms used in biomineralization and biological layer-by-layer assembly [2••,4,5,6,52]. Their superior properties are not trivially inferred from those of the components.

Catalysis could also benefit from optimized force balancing by implementing nano-confinement effects observed in biology. A case in point are molecular chaperones, which prevent aggregation of a number of proteins in crowded cells, and assist proteins to assume

their native conformation *in vivo*. The GroEL/GroES system in *E. coli* contains protein heptamers surrounding a nano-cage with a diameter of ∼4.5 nm [53]. Steric confinement helps proteins fold, thanks to periodic electrostatic interactions that result from a negatively charged internal surface during the time of folding. While the details are complicated, the GroEL/GroES system informs us on how different degrees of steric confinement, hydrophobicity, modulated surface charge and confined water content could be employed to tune protein stability [54,55,56•].

This insight can be applied to design catalysts consisting of nanostructured porous materials, such as SBA-15 silica, with constant, but tunable mesopore diameter, and enzymes immobilized on the pore surface. We recently observed that the catalytic activity of positively charged lysozyme or myoglobin, electrostatically adsorbed on the negatively charged pore surface of SBA-15, increased several times with respect to that of the free enzyme in aqueous solution, with minimal leaching [57•]. The highest activity was measured in SBA-15 with the narrowest pores. This smallest pore diameter (∼6 nm) barely exceeds the dimensions of lysozyme (3.0 nm × 3.0 nm × 4.5 nm) and myoglobin (2.9 nm × 3.6 nm × 6.4 nm), and approximates the cage diameter of GroEL. Confinement in nanopores not only allows us to tune catalytic activity, but it also facilitates enzyme recovery, may prevent denaturation, and improves thermal and environmental stability [58•]. Spectroscopic studies indicated that the balanced electrostatic–steric interactions prevent unfolding, by stabilizing the protein's native conformation [57•]. On the contrary, when the silica surface was functionalized with propyl groups, rendering it hydrophobic, the protein's conformation changed considerably, and activity dropped.

Computer simulations of polypeptides in nano-confining spaces provide clues on how confinement affects enzyme structure [59–61,62•,63]. The structure of confined water around enzymes in nanopores differs from that of bulk water, so that water-mediated interactions often affect the free energy landscape, and hereby enzyme stability [64,65•].

Electrostatics, steric confinement, hydrophobicity, and H-bonding all influence the activity and stability of enzymes. Mechanistic understanding of biological pores guide the design of artificial catalytic systems. In turn, studies of model nanostructured catalysts with tunable characteristics, like enzymes in functionalized SBA-15, advance our insight into biological systems.

Dynamic self-organization

Living systems are dynamic. A third opportunity for NICE lies in the time domain, essential to biological processes, to generate desired spatiotemporal behavior by synergy. Sometimes called 'emergence of complexity'

[66,67•,68••], robust properties collectively emerge from individual elements with much more basic functions. Dynamic structuring is rarely consciously applied in chemical engineering, and hardly in an optimal way. Nanotechnology and microtechnology opens avenues to realize [69•] what was originally only conceivable mathematically or on crystal surfaces [70,71,72•,73]. Learning how versatile, adaptable patterns emerge from biological system dynamics might guide new modes of reactor operation, and the design of new catalytic materials.

Periodic perturbation of a nonlinear system may form simple patterns [74••]. For example, the actions of water or wind create regularly spaced ridges on sandy beaches and dunes. Likewise, patterns develop when vibrating a plate covered by a thin layer of solid particles [75], an example of the rich, collective behavior of granular matter [76,77]. Energy is constantly provided to a nonlinear system, in which dissipation leads to pattern formation—an example of dynamic self-assembly [78••].

Hence, the idea to structure gas–solid fluidized beds by pulsing them with a periodically fluctuating gas flow, superimposed on a constant flow to maintain minimum fluidization [79•]. In a laterally thin, quasi-2D bed, this led to a hexagonally ordered array of rising bubbles, with a frequency that was half that of the pulsation, within a range of frequencies of a few Hz. Fluidized beds have complex hydrodynamics, which van den Bleek *et al.* [80] described as deterministically chaotic. By pulsing the gas, fluidization is more uniform, and channeling and clumping are prevented. This improves the performance of fluidized bed combustion and drying [81,82]. Periodically perturbing the gas in a fluidized bed can suppress chaos by 'phase locking' [83], however the periodicity of the bubble pattern is remarkable [79•]. In pulsed 3D beds, we observed patterns similar to those for vibrated granular media [79•,84]. While not as high as in quasi-2D beds, the patterns persisted in deeper beds than vibrated granular matter, due to less frictional dissipation. Interestingly, computational fluid dynamics (CFD) has not yet reproduced these experimental patterns, even though some level of structuring has been demonstrated [85]. We suggest that reproducing these patterns should be an interesting fingerprint to test CFD codes.

Other ways to stabilize a nonlinear dynamic system use closed-loop control. Hudson and co-workers [86] recently used (de-)synchronization methods to tune the collective response from weakly interacting rhythmic components, similar to those in biological systems, and applied them to control an electrochemical reaction system.

Bacterial communities present us with one of the most exciting examples of a dynamically self-organized system. Bacteria interact with their environment and each other, but are also self-propelling and self-replicating. Together,

they form complex communities that are more robust and adaptive than individual bacteria [87[•]]. When starved, they may self-organize into self-similar patterns [88,89], reminiscent of diffusion-limited aggregation (DLA) and other fractal aggregates seen in non-living systems [90], but their adaptive, collective behavior is richer. Bacterial communities attract interest in the context of biofilm research and engineering for chemical production [91]. They also stand model for other self-organizing systems, for example, in sociology [89].

Within the context of NICE, we see an opportunity to design artificial catalytic systems from elements that are not necessarily biological, yet use key aspects of bacterial communities. Building upon von Neumann's pioneering work on self-replicating automata, agent-based methods are ideally suited to explore the diversity of such bioinspired systems [92]. 'Agents' have internal states, can store energy and information, interact, sense and respond to their environment [66,93[•]]. Luisi and co-workers [94,95[•]] have explored the use of synthetic self-reproducing vesicles as minimal cells. This leads us to postulate that adaptive, self-replicating, internally or externally driven catalytic systems could be implemented, even based on purely artificial components.

Cooperative phenomena result from many interactions in a network of synergistic links [68[••]]. However, not all nodes and links are equally relevant. Some are more important, sensitive or robust than others. Collective behavior acts as an evolving, complex network [96–100], frequently with universal features, like scaling, clustering, and modularity [101[•]].

It would seem that insights in biological systems, reaction pathways and social networks, gained from topology, graph theory and information theory, could be useful not only in synthetic biology and process control, but also in generating more robust and adaptive bioinspired catalytic systems.

Conclusions

What makes biological organisms especially interesting from the viewpoint of chemical reaction engineering is that efficiency, scalability, robustness, and adaptability are quintessential to both, yet nature uses an arsenal of tools barely touched in engineering. In the context of recent progress, we have provided a personal view on how nature's hierarchical transport networks, force balancing and collective dynamics might be employed in reaction engineering design. At present, some fundamental mechanisms that serve biology so well are slowly permeating materials science and chemistry. However, they are scarcely applied in chemical reactor design and catalysis engineering.

Perhaps this is because we are rooted in an atomistic, bottom-up way of thinking that has helped us tremendously over the past century, yet we are confronted with a seemingly insurmountable gap between increasing nanoscale insights and capabilities, where rational design becomes a reality, and applications at the scale of macroscopic production, where empiricism seems inevitable.

Our examples show that this gap could be bridged by rational design principles based on nature-inspired chemical engineering, with the potential to transform what is too often and incorrectly considered a mature field, hereby helping to create sustainable processes. Such designs unite the atomistic and the holistic, using efficient mechanisms in natural systems as guidance for artificial designs—but not as models that are to be slavishly copied as automatically superior, without regard for context.

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