

## BIOLOGISTICS AND THE STRUGGLE FOR EFFICIENCY: CONCEPTS AND PERSPECTIVES

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The growth of world population, limitation of resources, economic problems, and environmental issues force engineers to develop increasingly efficient solutions for logistic systems. Pure optimization for efficiency, however, has often led to technical solutions that are vulnerable to variations in supply and demand, and to perturbations. In contrast, nature already provides a large variety of efficient, flexible, and robust logistic solutions. Can we utilize biological principles to design systems, which can flexibly adapt to hardly predictable, fluctuating conditions? We propose a bio-inspired “BioLogistics” approach to deduce dynamic organization processes and principles of adaptive self-control from biological systems, and to transfer them to man-made logistics (including nanologistics), using principles of modularity, self-assembly, self-organization, and decentralized coordination. Conversely, logistic models can help revealing the logic of biological processes at the systems level.

**Keywords:** Logistics; transportation; bio-inspired solutions; robustness; self-control; modularity.

### 1. Introduction

When the newly built Heathrow terminal 5 went into operation in 2008, it marked the beginning of a disaster: Thousands of lost luggage items were piling up rapidly, passengers were delayed, etc. It took about a week to fix the problem. In the complex logistic and supply systems of today’s highly connected, globalized world, similar systemic failures occur again and again. Triggered by insufficient responses to locally

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varying supplies or demands, a problem can quickly spread over large parts of the system. Examples for such problems range from blackouts of electric power grids up to the current crises of the automotive industry and the financial sector. This indicates that attempts to create highly efficient systems are often compromised by the sensitivity of large man-made structures to perturbations or varying demands, failures, or attacks.

Maximizing efficiency and profits often implies that redundancies and safety margins are minimized under the constraint that certain, yet acceptable failure rates are just kept. When connecting such systems to form larger ones, coincidences of failures, and their impact on a networked system are often underestimated. This is particularly true for so-called “complex systems” (where “complex” is to be distinguished from “complicated” and from “algorithmically complex,” i.e. computationally demanding). While many large logistic systems have all three properties, the complex systems we are focusing on are often characterized by nonlinear interactions of their elements and always by scalability issues. That is, size matters for the resulting outcome and dynamic behavior of the system [1]. Due to feedback loops and reinforcement effects, natural fluctuations in the system may trigger complex dynamics, instabilities, cascade failures, and regime shifts (i.e. transitions to a different state or operation mode). For example, variations in the distances of vehicles can trigger the breakdown of free flow, the formation of traffic jams (see video SV1), and even a *drop in road capacity*, which may cause a gridlock in large parts of the system [11].

## 2. Learning from Biology

Generally, the task of logistics as a key element of our modern, work-sharing economy is to make sure that required resources are delivered in the right quality and quantity to the requesting destination at the right time and acceptable costs. This involves the organization, management, and engineering of suitable technical systems. However, besides posing (NP-hard) problems, which may not anymore be solvable in real-time by brute force supercomputing, driving logistic systems towards maximum performance often drives them to an instability threshold, causing undesirable breakdowns. These are also known as “slower-is-faster effects” [11] (see the previous example of traffic). It is therefore evident that the struggle for efficiency in logistics is closely tied to the above-mentioned complexity challenge and that new solution strategies are needed.

Biological transport systems and their organizational principles could serve as an excellent source of inspiration for a variety of new solutions. In fact, logistics in the sense of the organization, coordination, and optimization of material flows, is a ubiquitous ingredient of biological systems, and bio-inspired approaches have often solved engineering problems in the past: A considerable number of natural structures and designs have been imitated under keywords such as “biomimicry,”

“biomimesis,” or “bionics” [3, 6, 34, 21]. Moreover, genetic algorithms and evolutionary optimization have been successfully applied to many problems, where exact optimization was not possible [26]. In contrast to previous bio-inspired approaches, which were primarily focused on imitating structural designs, we propose to concentrate on functional principles now, particularly on issues of dynamics and adaptive organization.

### 3. The Approach of BioLogistics

Analogies between biological and man-made logistic systems on the structural, functional, and dynamic level suggest a new, multi-disciplinary research field of “*BioLogistics*”, which connects biology with complexity science and engineering. The BioLogistics approach includes the derivation of innovative logistic solutions from successful strategies of nature as well as the analysis of biological systems from the logistics point of view. Of course, there are marked differences between biological systems and man-made logistics in terms of items and quantities, building blocks and mechanisms, designs and structures, topologies and scales, dynamics and growth, or organization and control (see supplementary Table 1). Nevertheless, it turns out to be fruitful to exploit the same vocabulary of design principles and properties such as resource-efficiency, robustness, adaptability, and noise control.

Biological logistic systems do an excellent job in using, distributing, and recycling sparse resources. Moreover, their efficiency and robustness to environmental perturbations are key to their survival. Millions of years of evolution have created logistic systems of such large variety and astonishing performance that one can hope to reveal a multitude of yet undiscovered functional designs and heuristic solutions. For example, cells have to produce or import, correctly transport, localize, and monitor the activity of thousands of different molecules. The human body even represents a “logistic universe” comparable with the phenomenal complexity of man-made global logistics: It manages to transport millions of different materials (nucleic acids, proteins, lipids, carbohydrates, and metabolites) to different destinations, establishing billions of molecular and cellular interactions (e.g. neuronal connections). This is done with an incredibly low energy consumption of a 60–100 Watts bulb ( $< 2,000$  kCal/day) and at very high reliability.

Understanding logistic processes in biology is, therefore, a new challenge. The current progress in cell biology can make big contributions to identifying molecular structures and regulation mechanisms. While the components of biological processes are being catalogued, we now need to unravel their dynamic interplay on the systems level. For example, how do biological systems respond to or even use variations in the concentrations of metabolites? A logistics view could largely help to reveal these dynamic interactions, and the systemic functions resulting from them. In recognition of the similarities between biological and man-made logistic systems, we will now introduce the BioLogistics approach by highlighting some key aspects concerning the infrastructure and organizational principles.

#### 4. Structure, Function, and Dynamic Organization

From a *structural* perspective, it is interesting to compare technological networks realizing logistics (such as distribution systems, vehicle, or data traffic) with biological networks: Remarkably, man-made and biological logistic networks share the same notions of transport infrastructure (roads, railways, or conveyor belts on the one hand, a cytoskeleton at the cellular scale or vascular system at the organism scale on the other). In both systems, we find mobile transport units and buffers for intermediate storage. Moreover, design principles of volume- or area-covering transport networks, respectively, seem to have universal features [4, 35]. This is the case, because both engineered and biological transport infrastructures minimize the use of resources under functional and physical constraints. Both aim to guarantee a reliable supply to all parts of the system, and to maximize transport efficiency.

From a *functional* perspective, we find again astonishing similarities between the two systems. For example, cellular traffic along cytoskeletal tracks (microtubules or actin filaments) may be compared with traffic along roads and highways. This shall be illustrated by Example 1.

##### Example 1: Intracellular traffic and crises in logistic transport

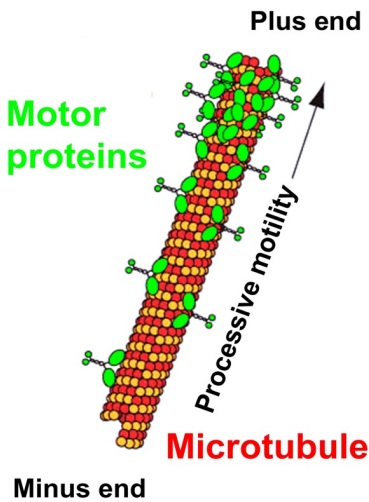
Most (eukaryotic) cells in nature comprise a cytoskeleton made up of filaments (such as microtubules, which have a diameter of about 25 nanometers and a length of several tens of micrometers). Apart from providing structural stability to the cell, these filaments serve as (multi-lane) tracks for motor proteins, which facilitate the long-range transport of various cargo (see video SV2). However, just as in urban and highway traffic (see Fig. 1(a)), high demand may lead to traffic jams, suboptimal throughput, and even collapse.

To avoid such states of crisis, cells have a number of control mechanisms at their disposal: the speed of cargo carried by molecular motors is influenced (i) by the composition of the surrounding solution, i.e. dependent on how much “fuel” (usually adenosine triphosphate, ATP) is provided, or whether there are specific inhibitors present, (ii) by the actual molecular structure of the motor itself, and (iii) by the “road conditions.” As such, optimal transport may be impeded by obstacles on the filament surface [19] or under conditions of motor crowding [33] (see Figs. 1(b) and 1(c)). Microtubule associated proteins (MAPs) can bind the microtubule surface independent of the motors. Once bound, MAPs may block the motor binding sites and influence the transport efficiency (i.e. cargo throughput). This kind of influence is part of the natural machinery of transport regulation [7]. However, if the MAP-concentration exceeds a certain threshold, transport may break down, leading the system into a state of crisis. Understanding the mechanisms behind such logistic crises may also allow the development of new therapeutic strategies for a number of diseases [2].

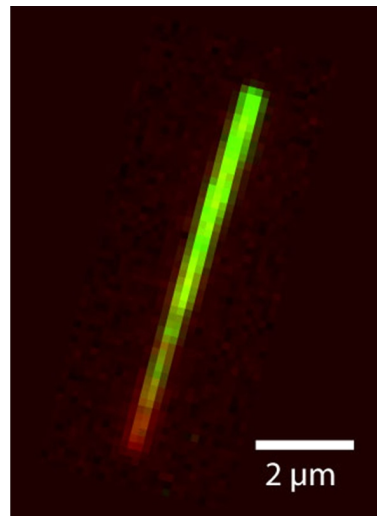
BioLogistics is particularly interested in analyzing the mechanisms, whereby cells cope with and avoid congestion. Such biologically inspired solutions will be useful for the improvement of man-made systems. However, BioLogistics shall also



(a)



(b)



(c)

Fig. 1. (a) Traffic jams on a road (see also video SV1). (b) Crowding effects along a microtubule in schematic representation. Motor proteins moving towards the microtubule plus end may form a concentration gradient and thereby cause crowding effects. (c) Experimental results for crowding effects depicted in (b). The image has been obtained by fluorescence microscopy of red-labeled microtubules and green-labeled motor proteins (adapted from Ref. 33). See also video SV1.

work the other way around: Logistic models can shed new light on biological processes and reveal their underlying mechanisms and dynamics. For example, they can help to understand the functional role that the crowding of motor proteins towards the microtubule plus ends may play (see Figs. 1(b) and (c)).

Both technical and biological logistic systems use multi-modal transport, i.e. a combination of different transport modes such as truck and railway traffic in distribution logistics, or diffusion and directed motion in the cell [13]. They perform the same functions like sorting, storage, and transport, which require mechanisms for item identification, destination search, routing, carrier choice, and delivery. Strategies for communication, coordination, and prioritization are essential as well. Furthermore, biological and man-made logistics seem to share pretty much the same goals, including cost efficiency, high throughput, spatial coverage, and robustness. The most important insights from biology, however, are expected from the perspective of *dynamic organization*, and its smooth interplay with the structural and functional level. As information technology becomes more powerful, efficiency challenges in logistics are increasingly addressed by a central control of production plans, quantities, time schedules, delivery times, and routes. This, however, may imply a low degree of flexibility with respect to varying conditions, a considerable sensitivity to perturbations, large administrative overheads and, sometimes, system breakdowns. Biological systems, in contrast, do not perform optimization in a strict sense. To understand why, we need to extend the notion of efficiency to the successful survival of a complex system in an uncertain and challenging environment. This includes the ability to respond to changing demands or sudden changes, and the maintenance of functionality under stressful conditions.

## 5. Success Strategies of Nature

Design principles of nature have to allow for flexible adaptation to requirements such as growth, shrinkage, or reorganization. The vascular system is a particularly well-known example, which has the ability to adapt to varying metabolic needs and body growth (see Example 2). The underlying success strategies include extensive recycling, self-organization, self-assembly [23, 36], and self-repair. These properties are largely based on local interactions, i.e. on decentralized control approaches [16, 24].

### Example 2: Sorting and distribution in engineered and biological systems

In engineered distribution networks, transport and sorting are usually well-separated: A fundamental principle of logistic systems is the use of economies of scale. As sorting is costly, sorting costs per item are minimized by having large-scale sorters in hubs (see Fig. 2(a)). All cargo from a certain region is transported to the hub, where it is sorted according to destinations, products, qualities, etc. Afterwards, it is shipped to the destination, often in a containerized way, without performing any other activity during the transport.

Biological systems, in contrast, tend to perform several functions in parallel. Examples of such multiplexing activities at the intracellular and multi-cellular scale are provided by endocytic and vascular networks. In a process called endocytosis, cells take up nutrients and signaling molecules from the outside. Whereas several

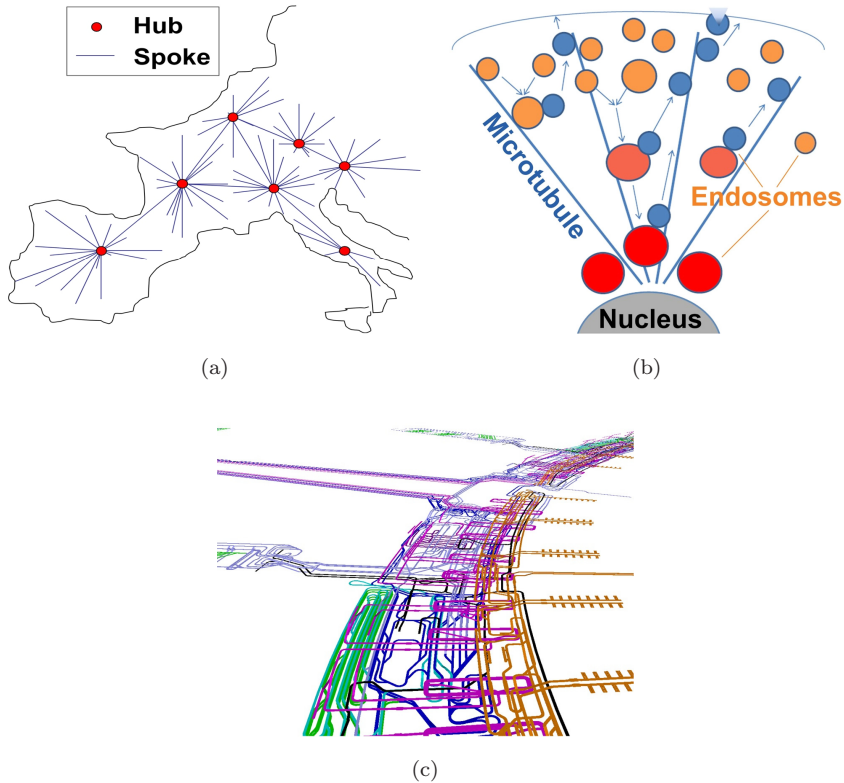


Fig. 2. (a) Illustration of a typical hub-and-spoke distribution network. (b) Schematic picture of the main processes during endocytosis (see also video SV3). (c) Illustration of a baggage handling system (BHS) used in airport baggage logistics.

types of cargo are transported to specialized compartments (lysosomes) for digestion, others (e.g. some cargo receptors) together with their containers can be recycled back to the surface of the cell to be re-utilized. Recycling is thus an important feature of cellular logistics. Cargo transport between the periphery and the cell center occurs concomitantly with cargo sorting and information exchange (signal transduction to the nucleus). This parallelism allows cells to carry out cargo transport and sorting on enormously compressed temporal and spatial scales, and to avoid overcrowding in transport processes towards the nucleus. The high logistic performance in the cell is reached by a combination of several processes (see Fig. 2(b) and video SV3): (1) fusion of small endosomes (“containers”) to form compact, larger ones, where cargo accumulates; (2) fission of endosomes to partially separate cargo to be transported towards the nucleus (for degradation) from cargo to be moved towards the cell surface (for recycling); (3) nonuniform motion, where periods of restricted movement alternate with periods of long-range transport [27]. Iterative repetitions of steps 1 and 2 during endosome movement facilitates to achieve high sorting quality and to keep control of cargo destination. Besides avoiding logistic



problems like crowdedness and traffic jams, the regulation of motility allows to trade off sorting quality and cargo delivery time. It will be interesting to determine under which conditions similar, bio-inspired solutions can outperform today's logistic systems. Furthermore, the optimal degree of centrality versus decentrality will be an important question to address.

Vascular networks also fulfill several functions simultaneously such as providing oxygen and nutrients to all cells in the body. They remove waste products, support immune defense, and serve communication, e.g. via growth factors and hormones. Moreover, they are highly adaptive to changing transport demands, and they have many things in common with baggage handling systems (BHSs) (see Fig. 2(c)). Therefore, it seems natural to transfer their design and operation principles to better adapt BHSs to varying transport volumes, changing origin–destination relations, and required system extensions, when the number of passengers increases.

Decentralized control approaches tend to scale better in terms of required control resources than centralized systems (see Example 3). Moreover, they are less sensitive to failures of system elements. Despite the prevalence of local interaction mechanisms in biological systems, however, decentralization is not a *general* rule, as the nervous system of higher organisms shows. Apparently, shortcuts between remote parts of a large, complex system are needed, when a local spreading of coordinated behavior would imply too large delays, which could cause unstable dynamics, loss of control, or system collapse.

To guarantee robustness, essential functions in biological systems are implemented in redundant ways (i.e. there is often a “plan B”). The body, for example, has alternative mechanisms of transport or of energy storage and provision. While these are often used in parallel to increase efficiency, in crises they may substitute each other. This redundancy also supports a large degree of autonomy and independence from specific environments and resources.

Last but not least, biological systems can cope well with fluctuations: While logistic operation in man-made systems typically fights fluctuations as undesired deviations from some planned behavior, biological systems often exploit fluctuations, e.g. for short-range transport via diffusion, or for innovation and evolutionary progress via mutations. Many functional states of biological systems are reached by self-organization, which makes them robust with respect to small fluctuations. In contrast, large fluctuations (in demand, for example) tend to trigger transitions to different system behaviors [24] (e.g. from metabolizing carbohydrates to burning fat). Many biological systems use such transitions for the adaptation to changed conditions like lower supply, and fluctuations are part of their functional design. In particular, fluctuations can support a reorganization of the system [31].

## 6. The Challenge of Putting BioLogistics to Practice

Could the above principles be exploited for a bio-inspired logistics? We definitely think so. But how can we optimize self-organizing systems that are prone to capacity



breakdowns when maximizing throughput? Example 3 describes an application to urban traffic flow control, which uses randomly occurring gaps in vehicle streams to serve other flow directions or other modes of transport. As a result, vehicles can enter the intersection according to a first-come-first-serve principle, when traffic volumes are low. At higher traffic flows, however, traffic lights form and serve *platoons* of vehicles, which is more efficient [22].

### Example 3: Centralized optimization versus self-control

When logistic or transport systems are designed and operated, it is quite common today to solve a related, multi-criterial optimization problem with powerful methods from Operations Research, considering costs, delays, or other criteria. This involves the maximization of a goal function. However, there are many possible ways of specifying the goal (e.g. to minimize costs or to maximize throughput), many possible boundary conditions (reflecting the assumed variability of prices and demands, or the distribution of transport volumes and destinations), and different scenarios (regarding situations that the system may face, e.g. certain failures). A system is usually optimized for a specific goal and expected typical conditions, but these conditions may never occur exactly. The goal may change as well, which may imply a significantly reduced performance as compared to the optimal operation that the system was designed for. Moreover, the behavior of complex systems is often hard to predict, and it may react in a sensitive way to external control. Under such conditions, a centralized feedback control (top-down approach), often requiring a supercomputer, may not be the best approach: It needs costly control structures and is sensitive to failures of the central unit due to errors or attacks. For so-called nonpolynomially hard (NP-hard, computationally demanding) problems, central performance is often insufficient for real-time optimization of large systems, which may cause information overload, negligence of potentially important information, and delay-induced instabilities. A common way to overcome this problem is to restrict the solution space, i.e. to introduce standard solutions suited for typical situations. This, however, reduces variability, which in turn affects the flexibility and adaptability to local or changing conditions. As a consequence, this may harm the efficiency and robustness of a system.

Coordinating vehicle flow and traffic lights in cities is a typical example for this problem [22] (see Fig. 3): At each traffic light, the order, duration, and starting times of green phases can be varied, resulting in a combinatorially large variety of possible solutions. The coordination of traffic streams is usually reached by restricting to cyclical signal operation, and by synchronizing these cycles. Optimal control strategies for an urban area are normally determined off-line, based on typical traffic conditions (say, for morning or evening rush hours). The control center switches between different standard control strategies, depending on the traffic conditions. Complementarily, green time durations may be adjusted locally. However, the traffic conditions, for which the signal schemes were optimized, never occur exactly. In fact, large fluctuations in the number of vehicles arriving during one cycle time make the traffic situation hard to predict. This can affect traffic performance considerably,

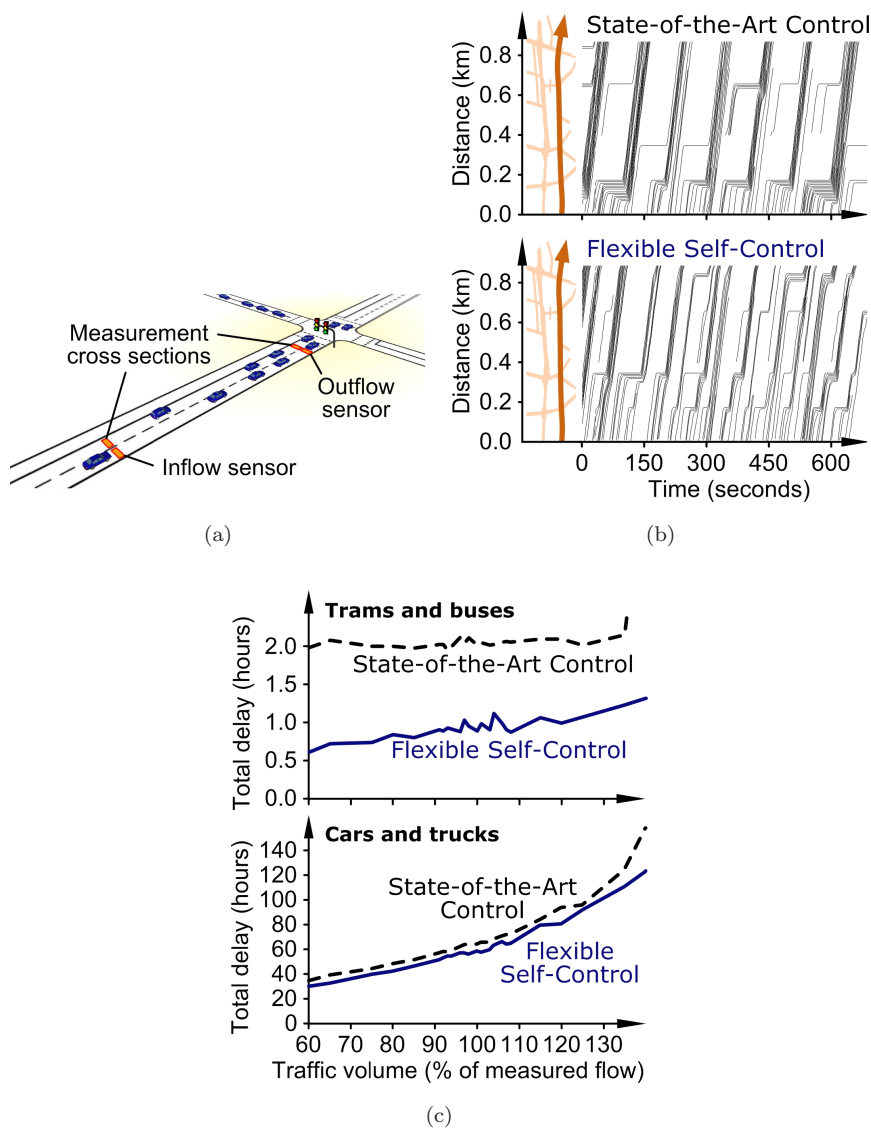


Fig. 3. (a) Traffic intersection with an inflow sensor to anticipate the arrival flow and an outflow sensor to determine the time when queues have resolved. Alternatively, one could use recently developed sensors, which are measuring traffic flows from above. (b) Vehicle trajectories along an arterial road. Top: State-of-the-art traffic control, implementing green waves based on a cyclical traffic light control. Bottom: Identical situation, but traffic lights are operated according to a self-organized control principle (see also video SV4). The resulting vehicle platoons are shorter and more irregular, so that traffic lights can use occurring gaps in the competing or intersecting flows and flexibly adjust to variations in the flows. (c) Resulting reduction in the total delay of trams or buses (top) and of other vehicles (bottom) as a function of the traffic volume.

in particular if road networks are heterogeneous and public transport is prioritized, which is normally the case. The problem is, therefore, to optimize a dynamic and strongly varying system, which can only be predicted over short time periods and reacts to control attempts very sensitively. Moreover, operating the system at maximum performance (capacity), as an optimization of throughput suggests, makes it vulnerable to breakdowns [11]: Delayed responses and dynamic feedbacks can trigger large-scale, cascade-like congestion spreading, i.e. systemic impacts, as perturbations in the flow of arriving vehicles may cause jammed road sections, which reduces the intersection capacity upstream and eventually produces gridlocks.

Problems like this occur in many complex systems, and the approach of BioLogistics can complement established Operations Research methods by revealing new heuristics for such challenges. One successful method suited for traffic light control, for example, is based on a pressure principle that produces self-organized oscillations. This method works as follows: Based on measurements of the inflows into the road sections (see Fig. 3(a)), one anticipates the vehicle flows that will arrive at the traffic lights a short time later. These anticipated flows allow one to determine the expected delays to all traffic streams, imposed by the respective traffic lights. Then, “traffic pressures” are defined by the temporal increase of the stream-specific cumulative delays, and at each intersection a green light is given to the traffic stream that exerts the highest traffic pressure. According to this principle, traffic streams control the traffic lights rather than the other way round. To avoid instabilities, growing queues are stabilized, whenever needed.

The resulting control principle is self-organized and decentralized (bottom-up approach). It reacts flexibly to the actual local situation rather than an average situation, and the short-term anticipation of vehicle flows reaches a coordination of neighboring traffic lights and vehicle streams (see Fig. 3(b)). In fact, self-control does not fight fluctuations in the flow by imposing a certain flow rhythm. It uses randomly appearing gaps in the flow to serve other traffic streams. According to simulation studies, this principle can reduce average delay times by 10%–30% (see Fig. 3(c)). The variation in travel times goes down as well, although the signal operation tends to be nonperiodic and, therefore, less predictable. Maximum acceptable red times and super-critical queue lengths are taken into account. Pedestrians are considered by virtual arrival flows, and trams or buses get a greater weight than vehicles.

In complex systems, it is often advantageous to support principles of *self-control* and *self-stabilization*, as is done by forthcoming traffic assistant systems [18]. Given the short-term predictability of the systems we are most interested in, strong, centralized control would potentially waste an unnecessarily high amount of resources for information gathering, transmission, processing, and control. It may also affect the adaptation of the system to changed conditions: If control is too forceful, the self-organization of autonomously operating elements, which naturally results from

nonlinear interactions, is overruled rather than efficiently used [24]. In order to profit from self-organization, a certain degree of variability must be tolerated to allow for flexible operation. In fact, rather than steadily forcing the system not to deviate from its planned behavior, which is costly, biology seems to apply the principle of “*guided self-organization*” or “*moderated self-control*” [12]: If the interactions between the system elements are suitable, only small feedback signals are necessary to reach the desired behavior. Hence, rather than strict forcing by a higher hierarchical level, the success principle is gentle interference (see, for example, the principle of “chaos control”) [16, 24]. This is usually based on the combination of antagonistic mechanisms, such as autocatalytic and inhibitory processes, or the combination of birth and death processes like fission and fusion (see Fig. 2). Antagonistic mechanisms are particularly important for growth and size control. If they are not well-balanced, the system can collapse or fail (see video SV3), or parts of it can expand in an uncontrolled way (cf. the example of cancer). The grand challenge of creating systems based on “guided self-organization” is the *design of suitable interaction mechanisms* between the system elements. For example, given a desired final structure, how should the parts and interactions in a self-assembly system be chosen? Self-organization *per se* does not cause optimal outcomes.

It must be avoided that the system gets stuck in a suboptimal, “frustrated” state, or that it behaves unstable, which could cause local breakdowns or even systemic failures. Some experience has recently been gained through the study of self-assembly [23], of self-organization in vehicle traffic and crowds [11], or through the design of peer-to-peer (P2P) systems [12]. Here, various kinds of coordination can spontaneously emerge by simple interactions [16, 24, 30]. Well-known examples are the synchronization of oscillatory processes or the establishment of cooperation between agents as studied by game theory [12].

Considering all this, focusing on bio-inspired solutions in logistic systems will establish a fruitful new research field, addressing challenges of complex systems characterized by nonlinear interactions of their constituents, delays, and possible breakdowns, where demand and other boundary conditions strongly fluctuate and are predictable only over short time periods. Circumstances like these are quite characteristic for economic and logistic systems on a national and global scale. Based on a better understanding of logistic design and operation principles in biology, it will be possible to improve engineered logistics by applying success principles of nature. BioLogistics also promises concepts for the construction of biological systems in bio-nano-engineering [14, 29], as is illustrated by Example 4. It is within reach to compose nanostructures, using intracellular transport and production mechanisms in synthetic cell-free environments. Moreover, it appears realistic to design structures by the cooperation of a large number of simple machines or robots [8, 20, 24, 30].

#### **Example 4: NanoLogistics**

Molecular shuttles based on motor proteins and cytoskeletal filaments have the potential to extend the lab-on-a-chip paradigm to nanofluidics by enabling the

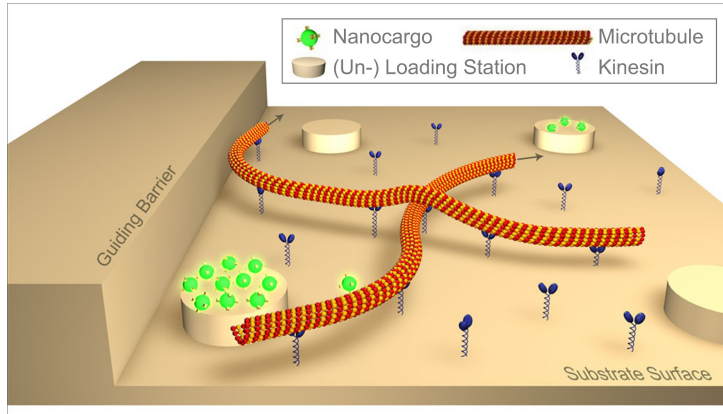


Fig. 4. Schematic illustration of a possible biomolecular transport system on the nanoscale. Microtubules are propelled over the surface of a silicon chip by immobilized kinesin motors (adapted from Ref. 17). Via specific linker molecules, the modular microtubule transporters may pick up cargo at a loading station and transport it to another location for unloading or sorting. To reliably guide the microtubule movement, chemical and topographical surface structures can be applied, the geometries of which mark the roads along which the flow of cargo is directed (see also video SV5).

active, directed and selective transport of molecules and nano-particles [9, 32]. In comparison with conventional nanotransport and nanomanipulation devices, biomolecular motors (i) are small and can therefore operate in a highly parallel manner, (ii) are easy to produce and can be modified by genetic engineering, and (iii) operate with high energy efficiency. One might envision that biomolecular motors could be used as molecule-sized robots (see Fig. 4) that (a) work in molecular factories, where small, but intricate structures are made on tiny assembly lines, (b) construct networks of molecular conductors and transistors for use as electrical circuits, or (c) continually patrol inside “adaptive” materials and repair them when necessary. Thus, biomolecular motors could form the basis of bottom-up approaches for the construction, active structuring, and maintenance at the nanometre scale.

In addition, artificial nanotransport systems provide an opportunity to simulate “real world” traffic and logistic scenarios. As such, it is conceivable to use molecular transport systems for the optimization of traffic routing or as biocomputation tools based on a combinatorial approach [25].

## 7. Modular Designs

Biological systems actually use large numbers of simple and small building blocks that are “cheap” to produce [24]. This facilitates modular designs [10], which do not require a *specific* unit to do a certain job: Any equivalent unit can do, which implies substitutability and robustness. Such modular logistic designs, which can reorganize quickly, become applicable to real problems now: Besides large-scale machines and equipment placed in fixed locations, recently, small multi-functional and mobile elements have become available to design future logistic systems. Their greater

flexibility results from the combinatorially large number of functions that can be performed in a cooperative manner. Furthermore, recent sensor and communication technologies allow engineers to implement adaptive self-control principles [15, 28, 30]. One successful example is the self-organized control of traffic lights [22]. Cooperative modular designs addressing future logistic problems could also put principles of swarm intelligence [5] into practice, as these can create complex and robust cooperative behavior from simple interactions. So far, logistics has not applied such concepts on a large scale. While solving related logistic challenges of the future, BioLogistics is expected to make many innovative contributions to these fields — for example, when creating self-controlled systems, in which machines and robots perform cooperative tasks [8, 20]. In essence, nonlinear interactions between the elements of complex systems pose great challenges for optimization and control. At the same time, however, they provide interesting new perspectives for self-stabilization and self-control.

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### Supplementary Information

The supplementary videos SV1 to SV5 and the supplementary Table 1 are available at <http://www.soms.ethz.ch/research/biologistics>.

### References

- [1] Anderson, P. W., More is different, *Science* **177** (1972) 393–396.
- [2] Aridor, M. and Hannan, L. A., Traffic jam: A compendium of human diseases that affect intracellular transport processes, *Traffic* **1** (2000) 836–851.
- [3] Ball, P., Life’s lessons in design, *Nature* **409** (2001) 413–416.
- [4] Banavar, J. R., Maritan, A. and Rinaldo, A., Size and form in efficient transportation networks, *Nature* **399** (1999) 130–132.
- [5] Bonabeau, E., Dorigo, M. and Theraulaz, G., Inspiration for optimization from social insect behaviour, *Nature* **406** (2000) 39–42.

- [6] Dickinson, M. H., Bionics: Biological insight into mechanical design, *Proc. Natl. Acad. Sci. USA* **96** (1999) 14208–14209.
- [7] Dixit, R., Ross, J. L., Goldman, Y. E. and Holzbaur, E. L. F., Differential regulation of dynein and kinesin motor proteins by tau, *Science* **319** (2008) 1086–1089.
- [8] Floreano, D. and Mattiussi, C., *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies* (MIT Press, Cambridge, 2008).
- [9] Goel, A. and Vogel, V., Harnessing biological motors to engineer systems for nanoscale transport and assembly, *Nature Nanotechnol.* **3** (2008) 465–475.
- [10] Hartwell, L. H., Hopfield, J. J., Leibler, S. and Murray, A. W., From molecular to modular cell biology, *Nature* **402** (1999) c47–C52.
- [11] Helbing, D., Traffic and related self-driven many-particle systems, *Rev. Mod. Phys.* **73** (2001) 1067–1141.
- [12] Helbing, D. (ed.), *Managing Complexity* (Springer, Berlin, 2008).
- [13] Helenius, J., Brouhard, G., Kalaidzidis, Y., Diez, S. and Howard, J., The depolymerizing kinesin MCAK uses lattice diffusion to rapidly target microtubule ends, *Nature* **441** (2006) 115–119.
- [14] Hess, H., Toward devices powered by biomolecular motors, *Science* **312** (2006) 860–861.
- [15] Hülsmann, M. and Windt, K. (eds.), *Understanding Autonomous Cooperation and Control in Logistics* (Springer, Berlin, 2007).
- [16] Kaneko, K., *Life: An Introduction to Complex Systems Biology* (Springer, Berlin, 2006).
- [17] Kersemakers, J., Ionov, L., Queitsch, U., Luna, S., Hess, H. and Diez, S., 3D Nanometer tracking of motile microtubules on reflective surfaces, *Small* **5**(15) (2009) 1732–1737.
- [18] Kesting, A., Treiber, M., Schönhof, M. and Helbing, D., Adaptive cruise control design for active congestion avoidance, *Transport. Res. C* **16**(6) (2008) 668–683.
- [19] Korten, T. and Diez, S., Setting up roadblocks for kinesin-1: Mechanism for the selective speed control of cargo carrying microtubules, *Lab Chip* **8** (2008) 1441–1447.
- [20] Krieger, M. J. B., Billeter, J.-B. and Keller, L., Ant-like task allocation and recruitment in cooperative robots, *Nature* **406** (2000) 992–995.
- [21] Kumar, S. and Bentley, P. (eds.), *On Growth, Form and Computers* (Academic Press, London, 2003).
- [22] Lämmer, S. and Helbing, D., Self-control of traffic lights and vehicle flows in urban road networks, *J. Stat. Mech.* (2008) P04019.
- [23] Li, M., Schnablegger, H. and Mann, S., Coupled synthesis and self-assembly of nanoparticles to give structures with controlled organization, *Nature* **402** (1999) 393–395.
- [24] Mikhailov, A. S. and Calenbuhr, V., *From Cells to Societies* (Springer, Berlin, 2006).
- [25] Nicolau, D. V., Nicolau, D. V., Jr., Solana, G., Hanson, K. L., Filipponi, L., Wang, L. S. and Lee, A. P., Molecular motors-based micro- and nano-biocomputation devices, *Microelectron. Eng.* **83** (2006) 1582–1588.
- [26] Passino, K. M., *Biomimicry for Optimization, Control, and Automation* (Springer, London, 2005).
- [27] Rink, J., Ghigo, E., Kalaidzidis, Y. and Zerial, M., Rab conversion as a mechanism of progression from early to late endosomes, *Cell* **122** (2005) 735–749.
- [28] Scholz-Reiter, B., Windt, K. and Freitag, M., Autonomous logistic processes — New demands and first approaches, in *Proc. 37th CIRP-ISMS* (2004), pp. 357–362.
- [29] Taton, T. A., Two-way traffic, *Nature Mater.* **2** (2003) 73–74.



- [30] Tumer, K. and Wolpert, D. (eds.), *Collectives and the Design of Complex Systems* (Springer, New York, 2004).
- [31] Ueda, K., Vaario, J. and Ohkura, K., Modelling of biological manufacturing systems for dynamic reconfiguration, *Annals CIRP* **46** (1997) 343–346.
- [32] van den Heuvel, M. G. and Dekker, C., Motor proteins at work for nanotechnology, *Science* **317** (2007) 333–336.
- [33] Varga, V., Helenius, J., Tanaka, K., Hyman, A. A., Tanaka, T. U. and Howard, J., Yeast kinesin-8 depolymerizes microtubules in a length-dependent manner, *Nature Cell Biol.* **8** (2006) 957–962.
- [34] Wadhawan, V. K., *Smart Structures* (Oxford University Press, Oxford, 2007).
- [35] West, G. B., Brown, J. H. and Enquist, B. J., The fourth dimension of life: Fractal geometry and allometric scaling of organisms, *Science* **284** (1999) 1677–1679.
- [36] Zhang, S., Fabrication of novel biomaterials through molecular self-assembly, *Nature Biotechnol.* **21** (2003) 1171–1178.