NETWORK SCIENCE

Destruction perfected

Pinpointing the nodes whose removal most effectively disrupts a network has become a lot easier with the development of an efficient algorithm. Potential applications might include cybersecurity and disease control. SEE LETTER P.65

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An enduring truth of network science is that the removal of a few highly connected nodes, or hubs, can break up a complex network into many disconnected components[1]. Sometimes, a fragmented and inactive network is more desirable than a functioning one. Consider, for example, the need to eliminate bacteria by disrupting their molecular network or by vaccinating a few individuals in a population to break up the contact network through which a pathogen spreads. In a quest to find the silver bullets that can effectively dismantle large networks, Morone and Makse[2] (page 65 of this issue) have developed an algorithm that achieves this by identifying sets of network nodes known as influencers.

It is not certain whether targeting and removing network hubs — defined as the nodes with the largest number of links — can inflict maximum disruption on a network. It may be more effective to eliminate a combination of hubs and central, but less-well-connected, nodes. The removal of hubs is usually preferred because they are easy to locate, whereas identifying the optimal set of nodes for which deletion would cause maximum damage is a non-deterministic polynomial-time hard (NP-hard) problem[3]. This means that it is computationally feasible only for small networks. Morone and Makse attack the problem of network disruption by mapping the integrity of a tree-like random network into optimal percolation[4,5] theory. From this, they derive an energy function with a minimum that corresponds to the set of nodes that need to be eliminated, to yield a network whose largest cluster is as small as possible. Although identifying this minimum is still an NP-hard problem, the authors were inspired by the energy function's shape to find a simple algorithm that offers an approximate solution.

To do this, Morone and Makse introduce the concept of collective influence, which is the product of the node's reduced degree (the number of its links minus one) and the sum of the reduced degrees of the nodes that are a certain number of steps away from it (Fig. 1). Collective influence describes how many other nodes can be reached from a given node, assuming that nodes of high collective influence have a crucial role in the network. The collective-influence-based algorithm then sequentially removes nodes, starting with those that have the highest collective influence (known as influencers) and recalculating the collective influence of the rest following each operation. The authors show that, for large networks, removing the set of influencers identified by this algorithm is more effective in fragmenting a network than removing the hubs, or than removing nodes that are identified through other algorithms, such as PageRank[6] or closeness centrality[7]. The set of influencers identified by the authors contains many nodes with few connections. This highlights the fact that the importance of a node in ensuring a network's integrity is determined not only by the number of direct links it has to other nodes, but also by which other nodes it is connected to.

The collective-influence algorithm is remarkable for its computational complexity because it requires only $N^2\log N$ computations to dismantle a network that contains N number of nodes. Its complexity is reduced to $N\log N$ if, instead of individual nodes, a fixed fraction of the total is removed at each step of the computation. The authors compare their method to the predictions of spin-glass theory, which was originally developed to describe the properties of disordered magnets and has found a range of applications in network analysis. They conclude that the nodes prioritized

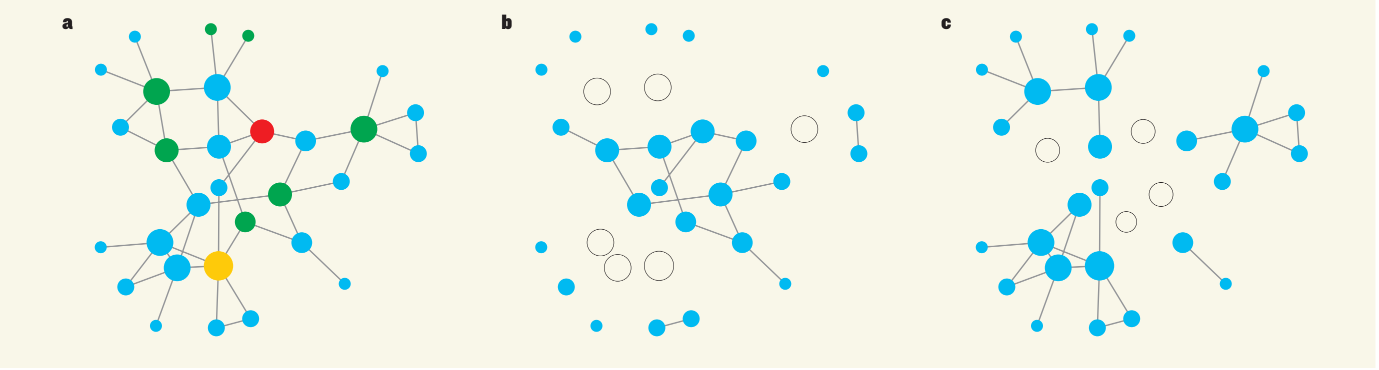

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Figure 1 | Optimal network demolition. Morone and Makse[2] introduce an algorithm that allows them to efficiently dismantle networks. The authors define the collective influence of a network node as the product of its reduced degree (the number of its nearest connections, k, minus one), and the total reduced degree of all nodes at distance d from it (defined as the number of steps from it). **a**, In this network, for $d=2$, the red node with $k=4$ has the highest collective influence, because the total reduced degree of the nodes at $d=2$ from it (green and yellow circles) is 21. This yields a collective influence of $3\times21=63$. The most connected hub, with $k=6$ (yellow circle), has a collective influence of 60. **b**, Removing the 6 nodes with the highest k (white circles) causes considerable damage to the network, but leaves a sub-network that contains 12 nodes unperturbed. **c**, By contrast, the algorithm developed by the authors allows them to identify a set of nodes (known as influencers) according to their collective influence. Using this, the removal of four influencer nodes (white circles) results in a fragmented network in which the largest connected cluster that remains has only ten nodes. This illustrates the algorithm's effectiveness over conventional methods for prioritizing network destruction.

by the collective-influence algorithm represent an approximate solution, which has a size close to that of the theoretical optimal solution. On the basis of spin-glass theory, we expect that the collective-influence solution has only a small overlap with the optimal solution, and hence must be treated with caution. However, the influencers found by collective influence are more effective in destroying a network than nodes selected by other methods. So even though the collective-influence method is approximate, it is faster and more efficient.

As with any new algorithm, open questions abound. The collective-influence algorithm has only one free parameter — the distance, expressed in the number of steps, from any given node. At zero distance, the collective influence of a node is equal to the square of its reduced degree, and so in this case the algorithm simply removes the hubs. To improve the algorithm's accuracy, one must choose a non-zero distance — but one that is not too large, because for large distances the boundaries of the network are reached, diminishing a node's collective influence (the collective influence approaches zero). Although Morone and Makse find that any distance greater than one works, a firm criterion for choosing an optimal value is lacking and would be desirable. Finally, because the authors designed their algorithm to work on networks that are locally tree-like, further work and quantitative evidence are needed on its expected accuracy for networks with loops, such as most social networks.

The collective-influence algorithm, just like similar algorithms, removes a node together with all its links. However, for many systems, node removal is too drastic an intervention. Softer touches, such as removing or rewiring specific links, are more tractable and desirable. For example, these approaches are relevant for networks in biological cells, in which many diseases are caused by mutations that result in deletion of links rather than the complete removal of nodes[8]. Understanding such 'edgetic' effects, and designing algorithms that can detect the minimum number of links to delete so as to achieve a given outcome, remains a challenge for future work.

The identification of optimal influencers, at either the node or the link level, is the first step towards building networks that would be robust against both attacks and failures. Mastering the design principles of such super-robust networks could have profound implications for anything from cybersecurity to the design of an attack- and error-tolerant power grid, and may even allow us to develop drugs that can rescue a cellular network from its diseased state with minimal side effects. ■

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DIABETES

A smart insulin patch

A microneedle-containing patch that is designed to sense elevated blood glucose levels and to respond by releasing insulin could offer people with diabetes a less-painful and more-reliable way to manage their condition.

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Diabetes is widely recognized as one of the biggest medical challenges of the twenty-first century, afflicting more than 280 million people globally[1]. People with diabetes must tirelessly self-monitor their blood glucose levels and inject the correct dose of the glucose-lowering hormone insulin to keep their blood glucose levels in the normal range[2]. This treatment regime involves challenges — it requires painful and inconvenient subcutaneous injections, is imprecise, and can cause serious problems if insulin dosage is not closely tuned to the patient's immediate physiological needs[3]. Reporting in *Proceedings of the National Academy of Sciences*, Yu *et al.*[4] describe a glucose-responsive microneedle patch that can be painlessly applied to the skin and that releases insulin as blood glucose levels increase.

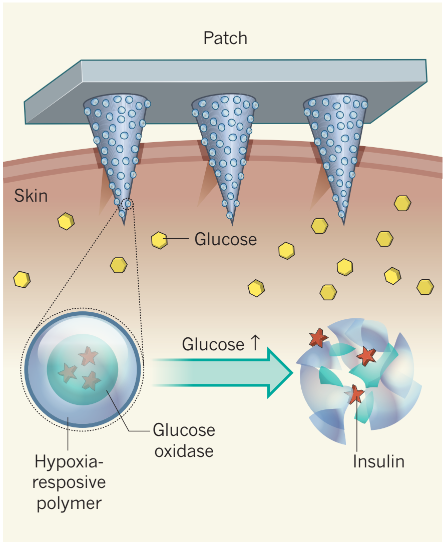

Figure 1 | A microneedle patch to monitor glucose and release insulin. Yu *et al.*[4] have developed a smart insulin-releasing patch made of 121 nanoparticle-containing microneedles. The patch painlessly penetrates the interstitial fluid between subcutaneous skin cells. The nanoparticles in each needle contain insulin and the glucose-sensing enzyme glucose oxidase, which converts glucose to gluconic acid. These molecules are surrounded by a hypoxia-responsive polymer. Increases in glucose oxidase activity in response to glucose elevation produce a low-oxygen environment in the nanoparticles, which is sensed by the hypoxia-responsive polymer, triggering disassembly of the nanoparticles and the release of insulin.

'Smart' glucose-responsive insulin-based therapies involve the automatic release of insulin in response to increases in blood glucose concentration. Smart therapies can improve disease control and limit the potential for excessively low blood glucose levels, which is a potentially deadly effect of excessive insulin dosing[3]. To mimic the physiological needs of a patient accurately, such therapies must respond rapidly to elevated glucose levels, and must release insulin with kinetics that closely mirror those of a healthy pancreas.

One type of smart therapy makes use of microcomputer-controlled insulin-delivery systems. These systems couple implantable continuous glucose monitors (CGMs) to automated pumps, and administer insulin through a subcutaneously inserted cannula tube. They are currently being evaluated in the clinic, and have shown promise in helping patients to achieve their target blood glucose level more regularly[5,6]. However, the sensors of current CGMs must be calibrated many times a day using hand-held glucometers. They produce blood-glucose measurements that lag behind true blood glucose levels by 5–15 minutes, hampering efforts to maintain a healthy range[3]. They are also the size of pagers, and the implanted sensors and cannula increase the risk of infection and require frequent maintenance and replacement to combat the body's immune response, increasing inconvenience, discomfort and cost to the patient[3].

The microneedle-patch device developed by Yu and colleagues is a 6-millimetre-square