Coming to an Airport Near You

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flux of reducing equivalents from respiration to formate production, because the *A. woodii* energy metabolism is strictly Na^+-dependent. HDCR can also use ferredoxin [a small protein that serves as energy currency in anaerobes (*9*)] as an electron donor, and ferredoxin can be reduced by carbon monoxide dehydrogenase (CODH), also present in *A. woodii*. By exploring this property, the authors observed CO_2 reduction from syngas either by coupling the two enzymes or using the whole-cell system. Syngas (which contains varying concentrations of H_2, CO, and CO_2) can be produced from gasification of wastes or biomass and is thus considered a renewable energy source. HDCR thus efficiently transforms H_2 and CO_2 (or syngas) into formic acid/formate, which can be used to generate energy by means of direct formic acid fuel cells (see the figure). These fuel cells operate at low temperature and are not far from commercial application for small mobile devices.

The HDCR enzyme also helps to elucidate the physiology of acetogens. Like other anaerobes, acetogens and methanogens live close to the thermodynamic limit of life, and their metabolism entails several thermodynamically unfavorable reactions. The most prominent of these is the reduction of ferredoxin by H_2 or NADH. A recent discovery transformed our understanding of the mechanisms used by these organisms to operate such difficult reactions (*9*). Buckel, Thauer, and co-workers have shown that an endergonic reaction (such as the reduction of ferredoxin by H_2) can be coupled to an exergonic reaction (such as the reduction of NAD^+ by H_2) through the splitting of the H_2 electron pair at a flavin cofactor (*9*). This electron bifurcation mechanism seems to be widespread in anaerobic microorganisms and is essential to both acetogens (*10*, *11*) and methanogens (*12*, *13*).

As Schuchmann and Müller show, HDCR is the single enzyme responsible for CO_2 reduction in *A. woodii*. Although it also interacts with ferredoxin, no electron bifurcation is involved, indicating that the organism usually encounters H_2 at partial pressures high enough to allow direct reduction of CO_2. This is in contrast to the hydrogenase–formate dehydrogenase complex from the Na^+-independent acetogen *Clostridium autoethanogenum*, which uses both NADPH and ferredoxin to reduce CO_2 in an electron confurcation process (the reverse mechanism of bifurcation, in which two electron donors are coupled to reduce one substrate) (*14*). Clearly, different energy conservation strategies are used by each organism. These exciting advances in anaerobic microbiology will go a long way toward helping to develop a sustainable H_2 economy that exploits microbial metabolic diversity for H_2 storage and production.

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EPIDEMIOLOGY

Coming to an Airport Near You

Definition of an effective distance between airports helps to explain the spread of epidemics across the global aviation network.

Angela R. McLean

Faced with the complexity of the global spread of new infections, a common approach has been to create enormous computer simulations (*1*, *2*). Most of these studies have yielded only tenuous insights, and scientific understanding has been slow to accrue. On page 1337 of this issue, Brockmann and Helbing (*3*) identify a useful metric—the effective distance—that helps to understand the spread of contagion across a travel network. Once this measure is specified, the global spread of infection can be understood as a simple reaction-diffusion process across the defined transportation network.

When a novel emerging infection appears, people ask themselves whether it will come to where they live and how long it will take to get there (*4*). Infectious diseases have long spread with travel and trade (*5*). Today, as the spread of SARS in 2003 and H1N1 influenza in 2009 illustrate, the global aviation network has become a potent disseminator of infections (*6*, *7*). However, geographical distance cannot explain the global spread of infection, because there are too many long-distance jumps across the air travel network. To overcome this problem, Brockmann and Helbing define an effective distance D_{eff} for any pair of airports in the global transportation network. For both simulated and past real epidemics, D_{eff} is a strong predictor of when a novel emerging infection will reach any given place from a specified starting point.

D_{eff} is driven by the proportion of people who leave one airport to go to another. Suppose you live in Busytown (*8*) and that 1% of people departing Nearbytown's airport arrive in Busytown, but only 0.01% of people who fly out of Faraway's airport land in Busytown. All other things being equal, a novel emerging infectious disease at Nearbytown poses a much greater threat to you than would the same disease at Faraway. This is the central idea of Brockmann and Helbing's D_{eff}, augmented with carefully crafted rules that define "shortest paths" for indirect journeys and formal models of the local spread of infection in the community served by each airport.

Once the effective distances between airports have been defined, the spread of infection across the global aviation network reduces to a simple reaction-diffusion process, with waves of infection propagating through a set of paths from one city to another. The new definition of distance explains quite precisely the speed at which SARS and H1N1 influenza spread to different countries around the world. Above all, from a plethora of detail and complexity of known facts about global travel, D_{eff} extracts the few things you need to know to answer the question "How long will 'it' take to get here?"

One of the powerful insights of this analysis is that the time to arrival of a new infection from one place to another is the prod-

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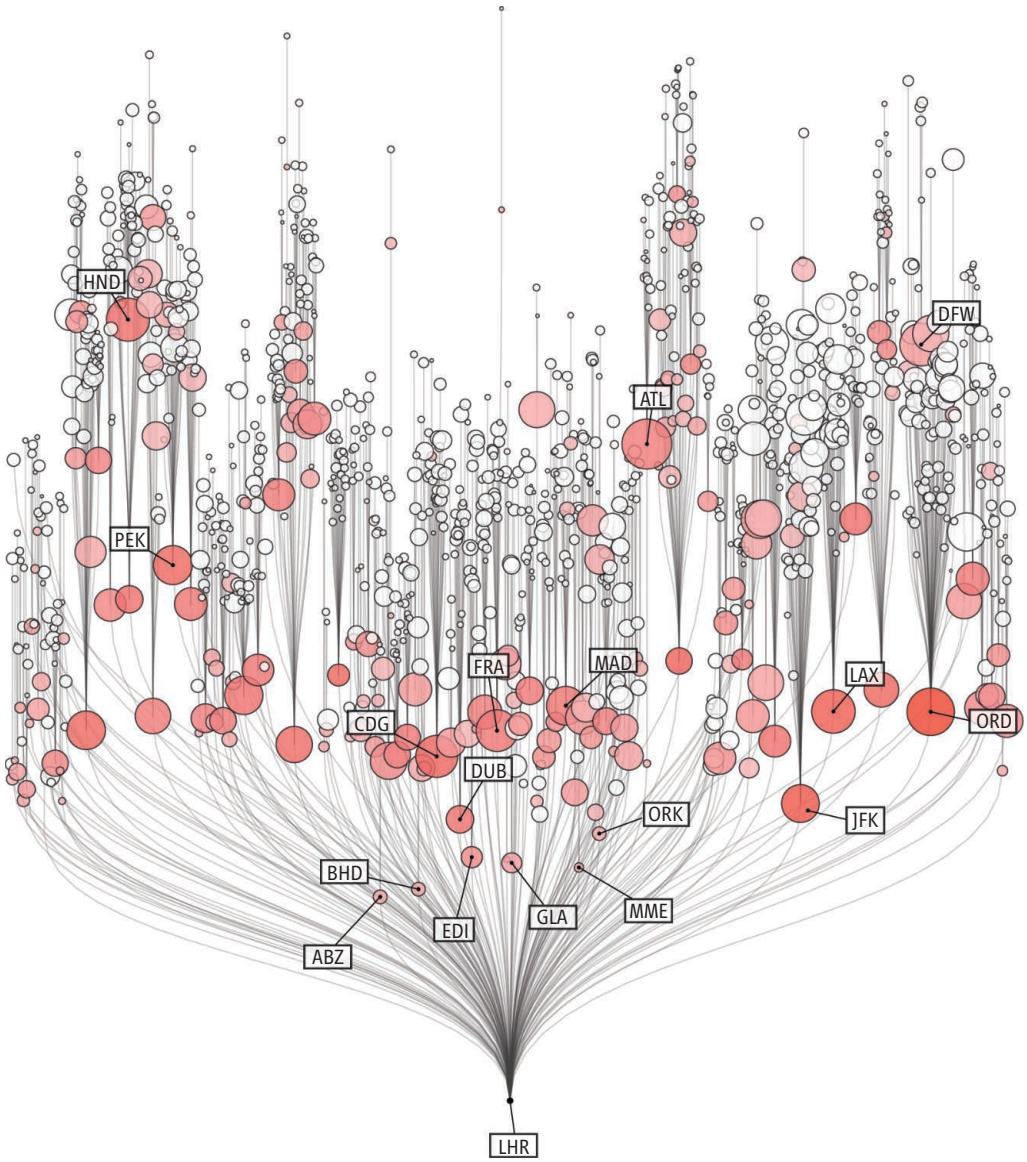

Who is coming to London? Brockmann and Helbing use the effective distance D_{eff} to illustrate where an infection might travel from a given location. A related (but different) version of D_{eff} measures how quickly a new emerging infection would arrive at an airport from another airport. As an example, the figure shows the shortest paths and effective distances from airports around the world to London Heathrow (LHR). Larger symbols have more traffic; darker symbols have more offspring branches in the tree. A small number of local UK airports such as Aberdeen (ABZ) and Glasgow (GLA) send a very large proportion of their passengers to London and are thus "close" according to this metric. Because Heathrow is a major hub in international travel, large airports such as those in New York (JFK), Los Angeles (LAX), and Beijing (PEK) are also "close" despite being geographically very distant. Other labeled airports are Atlanta (ATL), Belfast (BHD), Paris (CDG), Dallas (DFW), Dublin (DUB), Edinburgh (EDI), Frankfurt (FRA), Tokyo (HND), Madrid (MAD), Durham (MME), Chicago (ORD), and Cork (ORK).

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uct of two components: the effective distance between them and the velocity of the wavefront. The first of these depends only on the static underlying travel network; it is not altered by the particular parameters that define how fast a particular disease might spread. In contrast, the propagation speed depends only on disease-specific epidemiological parameters. This separation into the travel network and a particular epidemic spreading on that network creates a ranking of all airports in terms of the risk each one poses to any given location as an imminent source of new infection. If you sit in London and are responsible for monitoring the risks posed by new emerging infections, D_{eff} tells you years in advance which locations to watch with particular vigilance, because it defines the locations that would be the fastest to send you any novel infection (see the figure). D_{eff} (and the resulting risk ranking) changes on the relatively slow time scales at which the global aviation network evolves, not on the harried time scales of an unfolding international health emergency.

This elegant treatment of a complex problem does involve some simplifying assumptions. The modeling assumes that the number of passengers flying out of an airport is proportional to the size of the population served by that airport. Although this is a plausible assumption, it is not backed up by any data in Brockmann and Helbing's paper. This assumption needs testing with specific data on passenger traffic at various airports and the sizes of the populations they serve.

In recent years, network theories have been widely applied to explain the spread of epidemics (*9*). Such studies frequently assume (as do Brockmann and Helbing) that the underlying transmission network is fixed. For many networks, such as social interactions between individuals, that assumption is grossly restrictive. Perhaps one reason why Brockmann and Helbing's application of networks for epidemics seems to work so well is that it is reasonable to assume that the global aviation network is fixed, at least on the time scale of the spread of a pandemic. Given the projected growth of passenger numbers over the coming decades, this theory may be able to illuminate how much faster the next SARS or H1N1 will spread as more and more people take to the sky (*10*).

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