SOCIAL SCIENCE

The urban organism

Visitors to the area around *Nature*'s London offices will be familiar with the scene: unending traffic and noise; the hurly-burly of the Underground; streets, concourses and platforms filled with people intent only on reaching their destination quickly. It's received wisdom that the bigger a city is, the faster life moves; Luis Bettencourt and colleagues supply some empirical evidence to back up that perception (*Proc. Natl Acad. Sci. USA* **104,** 7301–7306; 2007).

The authors begin by examining how different indicators of cities' activity and infrastructure scale with their size. They use various sets of data from the United States, China and Germany, and characterize the scalings as power laws of the form (population)^n. They find that indicators of economic activity — from personal income, to patent registrations, to total electricity consumption — vary with population with values of n in the range 1.1–1.3, regardless of where the data were collected. In other words, cities the world over become more hyperactive the larger they get. Perhaps as a corollary to that excess, the prevalence of crime and sexually transmitted disease grows similarly quickly.

Infrastructure indicators such as the lengths of the road and electricity networks, by contrast, scale to around (population)$^{0.8}$. The larger the metropolis, the less of these things each citizen has at their disposal. Thus it seems that cities fulfill two basic needs of modern human society: they facilitate the exchange of ideas and, by extension, wealth creation; and they achieve economies of scale in the supply of a population's needs.

To look at how these very different dynamics affect city expansion over time, Bettencourt *et al.* construct a general equation that models the cost on resources of sustaining and increasing a population. Unsurprisingly, growth driven by the demands of efficiency, $n < 1$, stagnates after time: economies of scale eventually hit a bottom line.

City growth driven by wealth creation ($n > 1$), on the other hand, rapidly becomes hyperexponential. The only way to avoid collapse as a population outstrips the finite resources available to it is through constant waves of innovation. These effectively re-engineer the initial conditions of growth. But the greater the absolute population, the smaller the relative return on each such investment — so new ideas must come ever faster.

The city dweller looking for a quiet life is thus hit with a double whammy: the bigger the city, the faster life is; but the rate at which life gets faster must itself accelerate to maintain the city as a going concern.

In biological organisms, the authors note, the situation is completely different. Larger organisms have greater economies of scale, and slower-paced lives. Metabolic rates, for example, increase with (body mass)$^{0.75}$. With the city, it seems, mankind has created an organism operating beyond the bounds of what is natural. ■

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addition of a ubiquitin chain to Cdc20 by APC/C and UbcH10 does not necessarily involve protein degradation, but leads to the dissociation of Mad2 and BubR1 from Cdc20. One implication of this model is that APC/C would constantly antagonize its inhibition by the spindle-assembly checkpoint. If so, how could Mad2 and BubR1 ever inhibit the APC/C in cells with an active checkpoint?

A possible answer comes from a study carried out by Elledge's team[1]. In a search for proteins that are required for the activity of the spindle-assembly checkpoint, these authors identified a de-ubiquitinating enzyme known as USP44. Enzymes of this type disassemble ubiquitin chains by cleaving the bonds that connect the ubiquitin residues in the chain. Interestingly, USP44 differs from other known spindle-assembly checkpoint proteins in that it is not required to recruit Mad2 to unattached kinetochores, where Mad2 is believed to form complexes with Cdc20 and BubR1. So how else could USP44 function at the checkpoint? It turns out that, *in vitro*, USP44 can inhibit the ability of UbcH10 to activate checkpoint-inhibited APC/C, leading Elledge and colleagues to propose that USP44 might stabilize Cdc20–Mad2–BubR1 complexes by destroying the ubiquitin chains that APC/C adds to Cdc20 (Fig. 1b). Consistent with this argument, depletion of USP44 prematurely inactivates the spindle-assembly checkpoint in mitotic cells and leads to defects in chromosome segregation.

The model proposing that the stability of Cdc20–Mad2–BubR1 complexes is controlled by a fine balance between ubiquitination, mediated by the APC/C, and de-ubiquitination, catalysed by USP44, makes a number of predictions. Testing these will be an essential goal for the future. For example, could a mutant of Cdc20 be created that couldn't be ubiquitinated but would otherwise be functional? If so, such a mutant would be predicted to assemble into unusually stable checkpoint complexes from which Mad2 and BubR1 could not easily dissociate.

These studies[1,2] also raise a number of other questions. Is de-ubiquitinating Cdc20 the main role of USP44 in maintaining the spindle-assembly checkpoint, or does it also antagonize APC/C more directly by disassembling ubiquitin chains on its other protein substrates such as securin and cyclin B? How does ubiquitination dissociate Mad2 and BubR1 from Cdc20 — by inducing conformational changes in these proteins, or by recruiting enzymes (such as the p97/Cdc48–ATPase) that would catalyse the dissociation process? Finally, how is the balance between de-ubiquitination and ubiquitination reactions tipped once all chromosomes have become attached to both poles of the mitotic spindle? Elledge *et al.* found that USP44 itself is degraded at the end of cell division. Could this be the primary switch for checkpoint inactivation, or is it merely a consequence of APC/C activation once the checkpoint has been silenced? Answering these questions will keep researchers busy for some time to come. ■

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Correction
In the News & Views article "Cell biology: Lost in mitotic translation" by Anthony Wynshaw-Boris (*Nature* **446,** 274–275; 2007), statements in the text and the caption to Figure 1, and part **b** of Figure 1, imply that eIF4B binds directly to the 5′ cap of mRNA. Rather, eIF4B facilitates the ATP-dependent helicase activity of eIF4A to promote the ribosome recruitment necessary for cap-dependent translation.