are appropriately stimulated and remain sufficiently functional to generate these antimicrobial peptides. If so, defensin measurements could be useful in determining the optimal timing of antiviral therapy (*6*). The mechanism of the anti-HIV activity of defensins is of great interest, and may be mediated by defensins' effects on the viral particles, the host cells, or both.

In a companion paper by Biragyn *et al.* (*3*), we are introduced to yet another aspect of defensins: their ability to signal to the cells involved in adaptive immunity. In response to infection, defensins are produced within minutes to hours by neutrophils or specialized epithelial cells. Some defensins act as chemoattractants for immature dendritic cells (*7*) that present antigen to T cells when stimulated to mature. Biragyn and colleagues now show that murine β-defensin-2, in addition to being a chemoattractant that binds to and signals through the CCR6 chemokine receptor, also induces dendritic cells to mature by binding to Toll-like receptor-4. This receptor is essential for the host response to bacterial lipopolysaccharide (*8*). When the authors linked murine β-defensin-2 to nonimmunogenic tumor antigens, they obtained a potent cell-mediated immune response and antitumor activity in mice (*5*).

In this setting, defensins act as a potent immunological adjuvant, suggesting that they may be useful in the formulation of therapeutic antitumor vaccines for use in human cancer patients. However, defensin sequences vary considerably between humans, mice, and other animals, and it is not certain that a human defensin with similar properties will be found, or that the murine defensin will retain its activity in humans. More than 20 human defensin gene products remain uncharacterized and could provide useful leads in the search for functional homologs of murine β-defensin-2 (*9*).

We must assume (as the investigators do) that murine β-defensin-2 is not simply a highly efficient carrier for otherwise undetectable amounts of bacterial lipopolysaccharide. If we assume this, then we can infer that the defensin peptide exerts its effects through at least two unrelated receptors. The two main families of antimicrobial peptides found in humans, defensins and cathelicidins, are encoded by genes that have undergone rapid evolution, and there is little of the sequence conservation typically seen in peptides that are high-affinity ligands. Accordingly, the interactions of antimicrobial peptides with receptors are weaker than those of the primary ligands. Even though many antimicrobial peptides reach high concentrations in tissues and blood, it remains to be shown that their receptor-mediated activities take place naturally and are biologically important in vivo.

One possibility is that these highly variable cationic amphipathic peptides bind promiscuously to complementary pockets in other proteins, sometimes mimicking receptor ligands (*10*). Alternatively, the preferred targets of antimicrobial peptides in both microbes and host cells may be the lipid domains that surround membrane-associated proteins, including various mammalian receptors (*11*). Perhaps certain cationic amphipathic peptides mimic the combination of hydrophobic and polybasic motifs that anchor some receptors to anionic phospholipids in these lipid domains. The disruptive effects of murine β-defensin-2 on these lipid domains could produce an immunoadjuvant effect through the CCR6 and TLR-4 receptors. Better understanding of the interactions of antimicrobial peptides with different mammalian receptors may shed light on how these receptors operate, leading to new immunization strategies for preventing and treating cancer and other diseases.

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PERSPECTIVES: AURORAL AND SPACE PHYSICS

The Heavens in a Pile of Sand

Mervyn P. Freeman and Nicholas W. Watkins

Dramatic auroral displays over Earth's polar regions reveal a range of intricate patterns. Auroral spirals, westward-traveling surges, auroral curls, and many other phenomena have been identified on time scales from seconds to hours and spatial scales from 100 meters to thousands of kilometers (see the figure, panel A) (*1*). Recently, attention has begun to focus on whether there may be universal aspects to auroral structure, of the type observed in many complex natural systems (*2*).

One universal footprint seen in many complex systems is self-affinity. An object is self-affine if it is the same when viewed on any scale. In the early 1990s, the self-affinity of the aurora began to be noticed (3). Takalo *et al.* investigated this by analyzing the auroral electrojet (AE) index—a time series of the peak magnetic perturbation on the ground caused by electrical currents in the aurora, 100 km overhead (*4*). They found that the average squared difference between equally spaced points of the AE index time series doubled when the spacing was quadrupled, for any resolution between 1 and 100 min (*4*).

This fractional power law relationship is a classic definition of a self-affine structure—a "fractal." The fractal behavior was broken for time scales longer than 100 min, a feature thought to correspond to sporadic interruptions of the time series by a global auroral disturbance known as the substorm. Other measures of the AE index were also found to have power law relationships. For example, the probability distribution of the time for which the AE index exceeded a given fixed threshold followed a power law distribution from 1 to 1000 min. Superposed on the power law was another distribution centered on a fixed scale of ~100 min, corresponding to the substorm (*5*, *6*, *7*).

A similar measure was used to investigate the spatial structure of the aurora. In ultraviolet images of the aurora from NASA's Polar spacecraft, Lui *et al.* (*8*) identified auroral bright spots where the auroral emission intensity exceeded some fixed threshold, during both quiet and substorm intervals. They found a power law relationship between the number of bright spots and their area between 3000 and 1 million km^2. An additional population was found to be centered on a fixed scale of ~2 million km^2, corresponding to the substorm disturbance.

Because auroral bright spots evolve in space and time, a bright spot counted in one image at one time may be the same as another bright spot counted at an earlier or later time. Thus, the Lui *et al.* method overestimates the number of evolving spots. Uritsky *et al.* (*9*) reanalyzed Polar spacecraft auroral images, taking this spatiotemporal evolution into account (see the figure, panel B). The probability distribution of maximum bright spot area, and of area integrated over bright spot lifetime, now both followed a power law distribution over the entire observable range (three to five orders

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of magnitude). The probability distributions of bright spot lifetime, maximum dissipated power, and dissipated energy also followed power laws.

From these [and other (*5–7*)] observations, a picture has emerged of dynamically evolving "avalanches" of bright aurora with fractal structure in time and space. But why does nature paint such a picture? What is the answer in the auroral context to Kadanoff's famous question: "Fractals: Where's the physics?" (*10*).

Bak *et al.* (*11*) proposed that scale invariance in nature might be a result of self-organized criticality (SOC)—the tendency of slowly driven, interaction-dominated, thresholded systems to self-organize to a critical state, independent of the initial conditions. Here, the critical state is a statistically steady but nonequilibrium state in which the accumulating energy from the driver is released spasmodically in "avalanches" with a self-similar size distribution. This state arises from long-range correlations established through short-range interactions in a system with many degrees of freedom (*12*). SOC was first identified in computer experiments mimicking a slowly growing pile of sand and was experimentally established in a pile of rice (*13*).

The SOC paradigm has been applied to many natural systems, from earthquakes, measles, and forest fires to astrophysical accretion disks (*14*). Contemporary with the experimental work of Takalo *et al.*, several theorists recognized that criticality may offer an explanation for self-affine auroral structure (*5*, *6*). But why should the aurora behave like a sand pile (*6*)?

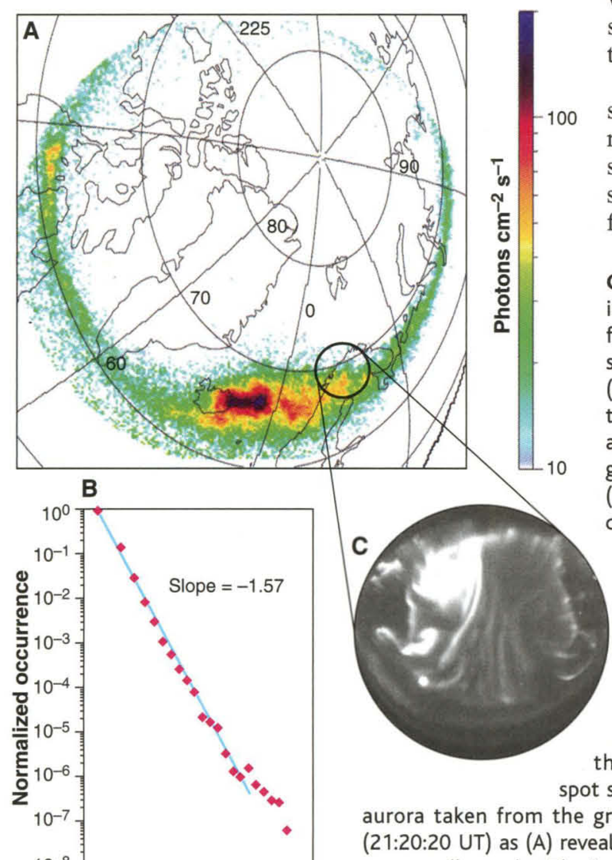
The aurora can be likened to a giant natural television screen. Charged particles from a natural electron gun in space are guided by Earth's magnetic field toward the polar atmosphere, where they collide with other particles and give off light. Thus, the aurora is a projection of the dynamic charged particle structure of the near-Earth space that is magnetically connected to Earth (a region known as the magnetosphere).

The collective dynamics of charged particles in a magnetic field is described by the equations of magnetohydrodynamics (MHD). Recently it has been shown that the MHD equations can be mapped onto discrete SOC equations (*15*). The scale-free structure of the aurora is then argued to come from a scale-free structure of a SOC magnetosphere. Indeed, satellite measurements in the magnetosphere have begun to show preliminary evidence of SOC in that fast flows of charged particles correlated with auroral emissions have a scale-free distribution of durations like that of SOC (*16*).

However, the scale-free structure of the aurora may not come from scale-free structure in the magnetosphere. Instead, it may arise from a similar scale-free structure in the turbulent solar wind that drives the magnetosphere (*7*). Studies using long (but non-overlapping) solar wind and auroral time series show the same static fractal properties, but comparisons using shorter but overlapping series could indicate that this may be coincidental rather than causal (*17*). Work continues on this issue, which is an example of a generic problem of complex systems coupled to complex drivers.

Another question, emphasized by Consolini and Chang (*5*), is how well the assumptions of the SOC model are met in the magnetosphere. In the original SOC models, scale-free behavior only emerged when the driving rate was very slow compared to the interaction time scales. However, another kind of nonequilibrium system exists in which the scale-free behavior only appears when the driving rate becomes sufficiently fast (*18*) (an example of forced criticality).

The debate between a driven and an internal origin for intermittent scale-free dynamics is not at all unique to the magnetosphere. It parallels a debate in theories of punctuated evolution between the influence of "external" events (such as asteroid impact) on extinctions and self-organized "internal" extinctions (*19*). Thus, complexity is providing a new approach to addressing long-standing space science problems, while in return space science is beginning to play an active role in addressing fundamental topical issues in complexity.



Complex beauty. (A) Ultraviolet image of Earth's aurora viewed from space by NASA's Polar satellite [21:19:23 universal time (UT), 16 February 1997]. Structures in the auroral luminosity are seen on many scales from the global to the image resolution (~20 km) and evolve on many different time scales. **(B)** When ~12,300 different evolving auroral spots above a given luminosity threshold were tracked (*9*), the number of bright spots of given maximum area followed a power law (a straight line when plotted with logarithmic axes). This means that there is no typical bright spot size. **(C)** An optical image of the aurora taken from the ground at about the same time (21:20:20 UT) as (A) reveals details of auroral structures to even smaller scales. The image radius is ~200 km centered above Kilpisjärvi, Finland. North is at the top of the image; the bright round spot in the southwest sky is the Moon.

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