

intertwined, it has remained unclear whether bleeding in embryos lacking tissue factor, PAR1, or other coagulation factors results from defective hemostasis or blood vessel formation. Griffin *et al.* now provide some insights by demonstrating that loss of PAR1 does not prevent vessel formation per se but rather impairs the stabilization and maturation of newly forming vessels, thereby causing breaches and abnormal fragility in the vessel walls (2). By switching on expression of PAR1 in endothelial cells, these investigators were able to rescue PAR1-deficient mouse embryos from bleeding to death. This demonstrates that activation of PAR1 and its signaling pathway in endothelial cells is essential for vascular integrity. By stimulating changes in endothelial cell shape, migration, and growth through enhancement of VEGF-dependent signaling, PAR1 may facilitate repair of vessel wall breaches and secure vascular integrity. Although the Griffin study, at first glance, seems to indicate that PAR1 affects only endothelial cells, endothelial PAR1 may also indirectly affect the recruitment, differentiation, interaction, or stabilization of perivascular cells (pericytes) by release of PDGF or matrix proteinase. Considering that ab-

normal vascular fragility is also apparent in embryos lacking angiopoietin-1, its Tie2 receptor, and several other angiogenic molecules (9), the interaction between coagulation and these angiogenic molecules deserves further study. Whether the vascular fragility in PAR1-deficient embryos results from defective thrombin or tissue factor/FVIIa/FXa signaling remains to be determined. Indeed, tissue factor is involved in the stabilization of newly forming fragile vessels, because loss of tissue factor causes vessel fragility owing to defective recruitment of pericytes (13).

Considering the pleiotropic activity of thrombin on vascular cells and its ability to trigger crucial angiogenic signaling by VEGF and HIF- α , why does loss of PAR1 impair stabilization but not growth of new vessels in the embryo? Even more important, to what extent do these findings in the embryo extrapolate to the adult, where angiogenesis contributes to, and coagulation factors are up-regulated in, numerous disorders? Surviving PAR1-deficient mice exhibit normal re-endothelialization after vascular injury, but we do not know whether angiogenesis in pathological conditions is impaired in mice with inactivated PAR genes. Coagulation factors are

likely to contribute to pathological angiogenesis because overexpression of tissue factor promotes tumor angiogenesis. Finally, even though coagulation factors and, in particular, PARs, have not been a direct target of pro- or anti-angiogenic drug development, they may become so in the future. Building stable vessels with PAR agonists would improve perfusion of ischemic tissues, whereas destabilizing vessels with PAR antagonists may suppress tumor growth. The observations of Griffin *et al.* should prime sufficient interest to ensure that these questions are answered in the near future.

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PERSPECTIVES: SOCIAL SCIENCE AND ECOLOGY

Networking Tips for Social Scientists and Ecologists

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For the past 30 years, a subdiscipline of the social sciences known as social network analysis has developed structural models to analyze human interactions (1). In social network analysis, discrete mathematics and statistics are combined with the emerging epistemology of complex systems to explore processes and phenomena as diverse as the diffusion of information through an organization, the adoption of innovations in society, and the spread of infectious disease in a population. Scientists working on social network analysis draw upon myriad disciplines: sociology, anthropology, psychology, geography, mathematics, statistics, and

computer science. Like social network analysis, analyses of trophic structure in ecological communities and of energy flow and nutrient transfer through ecosystems incur the problem of how to conceptualize and test interactions within these complex systems. The striking similarities between social networks and biological communities suggest that there exist constraining or structuring forces common to both. Social and ecological networks also share the need to reduce the elements and interactions of the network to an order simple enough to analyze, yet complex enough to reflect reality.

Simplifying complex system analysis was just one of the many topics discussed at an NSF-sponsored workshop on network theory and biocomplexity held at the Duke University Marine Laboratory in North Carolina (2). Computer scientist Stephen Seidman (Colorado State University) explained the social science concept of "cohesion" (how tightly knit a group of

people is) and the benefits of graph theory for delimiting nested networks in order to better understand influences within complex systems. The concept of cohesion parallels that of "guilds" (3) or "tropho-species" (4) in ecology, where organisms that eat and are eaten by similar species are treated as one group. Steven Borgatti (Boston College) and Martin Everett (University of Greenwich) discussed the concept and mathematical application of "regular equivalence," an approach to social networks that provides a formal model defining the notion of social roles. An example of regular equivalents would be two doctors at different hospitals. Although they do not see the same patients, or interact with the same suppliers, nurses, and administrators, they have similar interactions with equivalent others, and thus play the same role. Furthermore, their equivalence is decided not by their work or credentials per se, but by the relationships they have with other members of the network. Joseph Luczkovich (East Carolina University), an ecologist, demonstrated how regular equivalence, when applied to ecological communities, can help ecologists partition species into groups that play the same roles even if, unlike trophic guilds, they do not consume the same prey or share the same predators.

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Graphics software further aids in identifying groups of “actors” in social and ecological networks. One of the problems faced when visually rendering a large data set is the number of variables it contains. As every variable describes a dimension, visualization of many variables requires that the number of dimensions be reduced while preserving the information contained in the original data set. Once network structures are reduced to two or three key dimensions, they can

individuals participated in athletic activities, whether or not they hung out at the bar, and so on.

Johnson and colleagues (6, 7) have found MAGE to be valuable for visualizing food webs by applying regular equivalence and reducing the dimensions described in food web data. The resulting visualization looks remarkably like the food web presented by Neo Martinez (San Francisco State University) (8) that he constructed with Web3D software de-

trigued both social scientists and ecologists. Bernard Patten (University of Georgia) asserted that although ecologists are many decades away from understanding the complex behaviors of ecosystems, the advances made possible by interdisciplinary communication and collaboration signal a path toward progress.

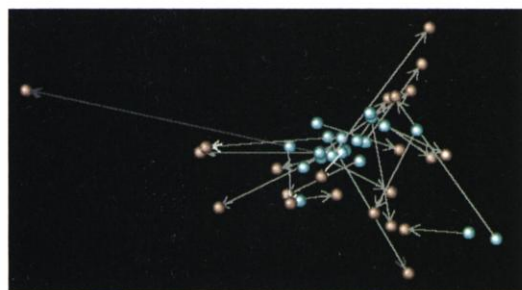
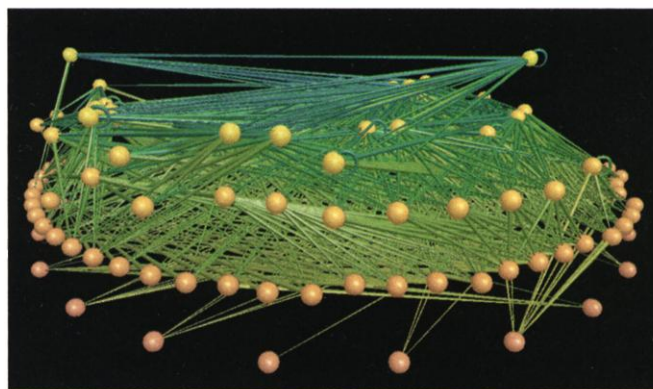
Tom Snijders (University of Groningen) presented work on the temporal evolution of social networks, emphasizing how continuous models can incorporate feedback loops that redefine the functions of the network. Kathleen Carley (Carnegie Mellon University) addressed this concept in her work on “multi-agent computational models” in which the modeled organization develops organically. In Carley’s analysis of corporate structures, she found that social structure (who talks to whom), reporting structure (who reports to whom), and the knowledge network (who knows what) coevolve, resulting in emerging roles and evolving behaviors within the organization. One example would be the emergence of a leader from a leaderless group because of the information pathways within that group. Robert Ulanowicz (University of Maryland) discussed similar emergent processes in the form of autocatalytic behaviors (self-organizing feedback) in ecosystems. An example of an autocatalytic behavior would be the strengthening of the overall cohesion among interacting species because the “end link in the chain benefits the beginning link.”

These efforts as well as other projects presented at the conference demonstrate that on many scales, social scientists, biologists, and physicists are all studying the same phenomenon. Most of the difficult problems modern society faces arrive in the form of complex structures such as economies, ecosystems, and societies. Interactions among social scientists and biologists and the integration of their techniques and insights may prove crucial to developing a new understanding of how these complex systems behave.

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(Top) A food web of Little Rock Lake, developed with Web3D, displays the feeding links between lake organisms across trophic levels. Different-colored nodes represent different trophic levels. The darker (redder) the node, the lower on the trophic chain that node is. Thus, there are more herbivores (dark orange) than primary producers (red), and the top predators (bright yellow) seem to be generalists, as they are each connected to quite a few lower nodes. Green rings represent cannibals. **(Bottom)** A correspondence analysis of stacked matrices using MAGE software compares an actor’s position (social role relative to the rest of the group) in March (beginning of winter, blue) and October (end of winter, brown) at an Antarctic research station. All persons are described by two dots (or positions). The first (blue) is how they stand with respect to all others (based on surveys of relatedness) at the beginning of winter. The second (brown) is how they are positioned in relation to others at the end of winter. The trend from a cohesive to a divisive network structure (tightly clustered to widely distributed) is readily apparent in the MAGE output.



be visualized using graphics software. MAGE (5), a program designed by Duke University biochemists David and Jane Richardson to help molecular biologists visualize complex molecules, has been adapted by Jeffrey Johnson (East Carolina University) to study social networks at an Antarctic research station over several winters (see the figure, bottom). The software helped Johnson visualize the social interactions among teams of overwintering scientists, technicians, and support staff. The structure depicts how close or distant each member was from the others, how activities, habits, and tasks within the group influenced the entire group, and how these relationships changed over time. MAGE allowed visualization of changes in group cohesion as determined by the sum total of social interactions—for example, whether or not

developed by Richard J. Williams (San Francisco State University) (see the figure, top). Although MAGE and Web3D software analyze complex systems differently, each program emphasizes unique patterns of interactions that can be interpreted and then tested. Martinez pointed out that “ecologists can use social science software to analyze species ‘betweenness’ and ‘degrees of separation,’ [while] social scientists can use ecological software to visualize and comparatively measure the complexity of social networks using ‘connectance.’”

One of the lingering problems in network analysis is the dynamic behavior of complex networks. How do changes in networks over spatial and temporal scales rewrite the rules that produced the network structure in the first place? The difficulty in examining dynamic networks has in-