Experimenting with Buddies

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mutant form smaller tumors in mice than cells expressing wild-type PKM2. This difference in growth was rescued by treatment of mice with the antioxidant *N*-acetylcysteine, which is a precursor for glutathione synthesis. The results suggest that small-molecule activators of PKM2 that limit the ability of glycolytic intermediates to fuel the pentose phosphate pathway, coupled with radiation or chemotherapeutic drugs that increase oxidative stress, may promote high levels of oxidative stress, which are toxic to cancer cells.

PKM2 is also expressed in nontransformed cells, including stem cells (*10*), which are exquisitely sensitive to oxidative stress. Stem cells proliferate slowly, reside in hypoxic niches, and display robust glucose metabolism (*11*). This high rate of glucose metabolism is supported by the transcription factor HIF-1, which promotes glycolysis while inhibiting oxidative phosphorylation. Interestingly, PKM2 localizes to the nucleus, where it interacts with HIF-1 and promotes the expression of HIF-1 target genes (*12*). PKM2 also interacts with β-catenin and OCT-4, two factors important for stem cell maintenance, highlighting the diverse roles of PKM2 in this capacity (*13*, *14*). It is unclear whether these nuclear functions of PKM2 are affected by cysteine oxidation, or whether the redox buffering role of PKM2 is important in other nontransformed cells that express PKM2.

Regulation of the pentose phosphate pathway to promote cellular redox balance is not limited to mammals. The yeast *Saccharomyces cerevisiae* switches pyruvate kinase isoforms from the high-flux PYK1 when grown on fermentable carbon sources to the low-flux PYK2 when grown on oxidizable carbon sources. Low pyruvate kinase activity in yeast promotes flux through the pentose phosphate pathway, promoting NADPH production and protecting yeast from oxidative damage caused by mitochondrial ROS generation during respiration (*15*). Thus, expression of low-activity isoforms of pyruvate kinase seems to be an evolutionarily conserved mechanism to promote cellular redox homeostasis.

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SOCIOLOGY

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Internet experiments start to unravel the role of social networks in the spread of behavior in society.

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Go to any social gathering in your neighborhood and you will notice that people interact mostly with others who are similar in terms of age, gender, race, attributes, and behaviors. This tendency of people to have similar friends—known as homophily—is one of the most pervasive features of social networks (*1*). A key question is how much of the homophily in behavior can be attributed to social diffusion, that is, direct causal influence of one person on another through social ties (*2*, *3*). Results from two clever Internet experiments reported by Centola last year (*4*) and on page 1269 of this issue (*5*) shed light on how the particular arrangement of social ties promotes social diffusion.

Observational studies on real-world behavioral diffusion cannot disentangle social contagion, homophily, and friendship formation (*6*, *7*). Therefore, social scientists would like to conduct randomized controlled experiments instead, as is standard in biomedical research. Although some network experiments have been carried out (*8*–*10*), Centola's Internet experiments come closest to the ideal of a non-artificial randomized experiment, in which the network structure is fully controlled by the experimenter.

For his studies, Centola devised a professional-looking social network Web site to promote health and fitness. Subjects were attracted to this site through advertisements on health Web sites. At registration, each subject chose a username and avatar and was assigned six other subjects, his or her "health buddies," whose characteristics and activities the subject could observe during participation. When a subject started a new activity, his or her buddies were invited to also participate in this activity. The experimenter controlled the matching of health buddies and ensured that, after introduction, subjects only learned about the new activity through their health buddies. This setup enforced social diffusion of the new activity and allowed the experimenter to analyze the effect of different health buddy assignments on the level of social diffusion.

The experimental design in last year's study randomly assigned subjects to two conditions: one in which the matching of health buddies formed a clustered network (see the figure, panel A), and another in which the matching formed a random network (see the figure, panel B). In each network, health buddies of an initial dummy subject received a personalized invitation to register for a health forum. Acceptance triggered a new round of invitations to the health buddies of those who registered, and so on, leading to diffusion of the health forum registration through the network.

The results were surprising. Centola found that diffusion reached more subjects in the clustered networks than in the random networks, whereas standard percolation or epidemiological diffusion models would predict the opposite. However, in these models, one node can infect each of its neighbors with equal probability, whereas in social diffusion, two or more "infected" friends are often required to persuade an exposed subject to adopt his or her friends' behavior.

Centola's present results are equally surprising. This time, buddy matching imposed exactly the same network structure on both conditions, but levels of homophily differed: In one condition, no homophily bias was

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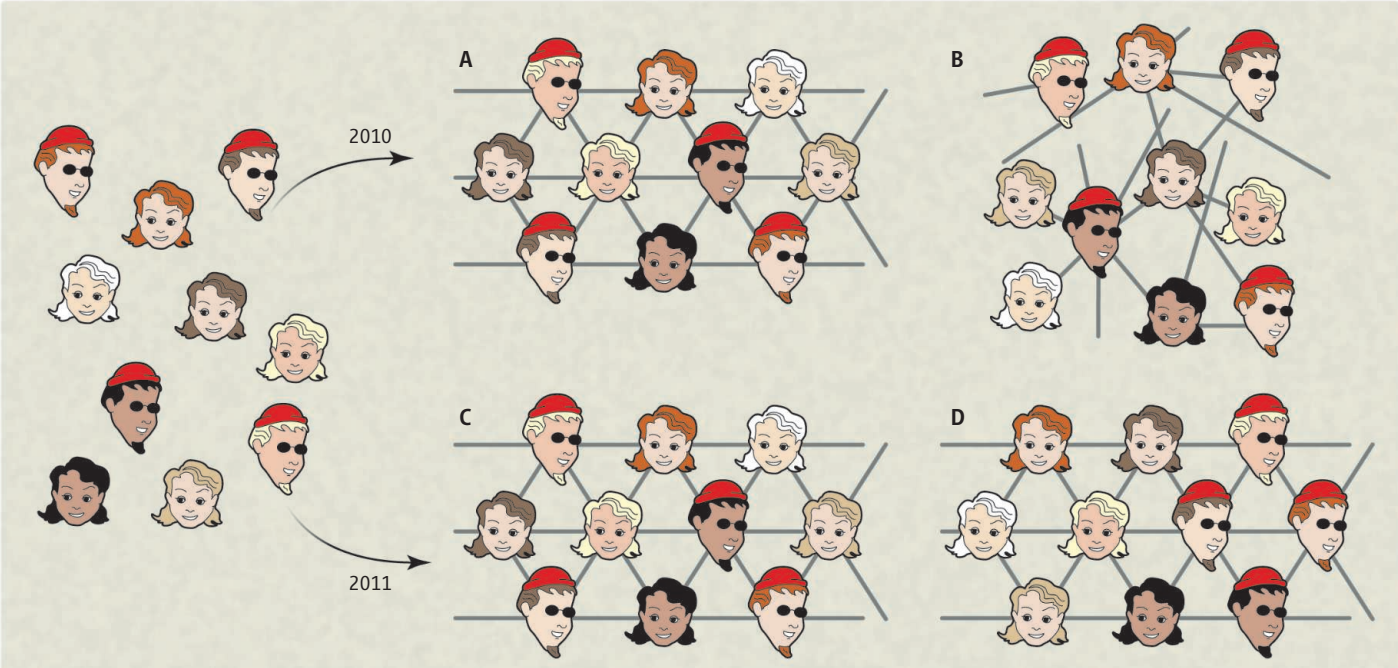

Testing for social diffusion. In a study published last year, Centola (*4*) assigned subjects randomly to (**A**) a clustered lattice network or (**B**) a random network. In both networks there was no homophily. In this issue (*5*), the author uses a different experimental setup: Subjects are randomly assigned to either (**C**) a network without homophily or (**D**) a network with homophily; the network structure is the same in both conditions. The actual networks in the design were much larger than illustrated here.

imposed (see the figure, panel C), whereas in the other, buddies were matched in terms of gender, age, and body mass index (see the figure, panel D). A diet diary was introduced to a dummy subject, and its health buddies were invited to sign up for the diet diary as well. Adoption of the diet diary triggered further invitations to adopters' health buddies, spreading the diary through the network. Diffusion levels were tracked, and were observed to be much higher in the network with homophily than in the nonhomophilous network.

Previous studies have indicated that homophily may lead to quicker initial diffusion by improving communication, but that homophily could also lead to greater inequality; diffusion may get trapped in the community of the initial adopters (*11*, *12*). This trap never happened in Centola's study. On the contrary, although the diet diary was introduced to a non-obese seed, the obese subjects benefited most from the homophily treatment.

The results raise questions about the current approach toward analyzing homophily and social diffusion. Researchers studying this topic typically first generate homophilous network structures according to some network formation process, and then consider some social diffusion process on the generated network structures (*12*, *13*).

This approach has two problems. First, it considers "homophily" (people have friendships with similar others) to be equal to "homophilous network formation" (people form friendships with similar others), although they are not the same. A network formation process with a homophily bias simultaneously induces homophily and more community structure in the network. More bias may indeed induce lower diffusion levels, but this might as well be attributed to the change in network structure as to the change in the level of homophily.

Second, in standard diffusion processes each tie has equal weight in the diffusion process, but Centola's experimental results suggest that similar friends are more influential. Centola develops a theoretical diffusion model in which diffusion only proceeds through homophilous ties and shows that his model captures the diffusion pattern well.

Centola's results suggest that introducing homophily promotes social diffusion, but how general are these results? Diffusion of binary behavior, such as the adoption of an innovation, is quite different from diffusion of a behavior on a continuous variable, such as the time invested in some activity (*13*). The latter is usually modeled as a linear updating process, and whether the results hold under this kind of process remains to be seen. Centola's experimental design explicitly separated network structure from homophily, but in general, experimenters are free to correlate homophily and network structure in their designs. This leads us to a general optimization question: For a given diffusion process, what is the best arrangement of network ties and assignment of subjects to nodes, such that diffusion levels are highest? The answer should be of considerable interest for policy-makers and for marketing and social media managers. Centola's results suggest that it is possible for policy-makers to reach policy goals by designing social network Web sites and cleverly arranging the social ties within. This should be an encouragement to policy-makers and social science researchers alike.

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