

18. G. Zhang, J. Zhang, S. Liu, *J. Atmos. Chem.* **57**, 41 (2007).
19. G. Onitsuka, I. Uno, T. Yanagi, J.-H. Yoon, *J. Oceanogr.* **65**, 433 (2009).
20. J. Kang, B. C. Cho, C. B. Lee, *Sci. Total Environ.* **408**, 2369 (2010).
21. Seawater N^* values in the euphotic layer were affected by the supply of N from the upper thermocline (formed by remineralization of organic matter), which occurs on time scales less than 1 year; this is in contrast to the monthly time scale on which the atmospheric nitrogen supply into the euphotic layer was measured. The mismatch in time scales of these two processes (N supply from below versus air- N^{ANTH} deposition) could affect the correlations between the values of surface N^* and air- N^{ANTH} deposition. Therefore, to remove seasonal fluctuations and to highlight the interannual or long-term trends, the data for air- N^{ANTH} deposition and seawater N^* were smoothed using a 2-year moving average before undertaking comparisons. This data treatment minimized potential biases in the correlations in Fig. 3, enabling comparison of the two parameters.
22. P. G. Falkowski, R. T. Barber, V. Smetacek, *Science* **281**, 200 (1998).
23. Y. W. Watanabe, M. Shigemitsu, K. Tadokoro, *Geophys. Res. Lett.* **35**, L01602 (2008).
24. The riverine influence is largely confined to Chinese coastal waters during winter (October to April), whereas, in summer (May to September), the freshwater plume extends northeast toward Cheju Island (on which an air-monitoring station, marked "A" in Fig. 3E, is located) (30). However, the impact of the river plume rapidly diminished away from the source, as indicated by a rapid decrease in N concentration from 40 μM at the mouth of the Changjiang River to 3 μM in offshore waters, ~300 km distant from the river mouth (Fig. 3F) (31). About 75% of the total nitrogen load from the Changjiang River is added to the East China Sea during summer, with the remainder added during winter (32). In addition, we found no statistically significant correlations between seawater N^* values in boxes 6 and 7 (wherein the effect of the Han River is likely strong) and N^* values measured over the past 15 years in waters near the mouth of the Han River (fig. S6), indicating a negligible contribution from the Han River nitrogen flux into the Yellow Sea.
25. Contributions from N_2 fixation are unlikely because oceanic conditions in our study area did not favor N_2 fixation. With rare exceptions (33, 34), most N_2 fixation blooms occur in tropical oceans in which the fixed N concentration is nearly zero and the sea surface temperature is generally higher than 25°C (35, 36). Most of our study areas featured sea surface temperatures below 25°C, except during the summer season, and the surface N concentrations were generally greater than the detection limits.
26. S. C. Doney, *Science* **328**, 1512 (2010).
27. C. A. Klausmeier, E. Litchman, T. Daufresne, S. A. Levin, *Nature* **429**, 171 (2004).
28. K. R. Arrigo, *Nature* **437**, 349 (2005).
29. T. S. Weber, C. Deutsch, *Nature* **467**, 550 (2010).
30. H. Ichikawa, R. C. Beardsley, *J. Oceanogr.* **58**, 77 (2002).
31. B. D. Wang, X. L. Wang, R. Zhan, *Estuar. Coast. Shelf Sci.* **58**, 127 (2003).
32. Z. Dai, J. Du, X. Zhang, N. Su, J. Li, *Environ. Sci. Technol.* **45**, 223 (2011).
33. G. H. Park *et al.*, *Limnol. Oceanogr.* **53**, 1697 (2008).
34. P. H. Moisander *et al.*, *Science* **327**, 1512 (2010).
35. D. Karl *et al.*, *Biogeochemistry* **57-58**, 47 (2002).
36. C. S. Davis, D. J. McGillicuddy Jr., *Science* **312**, 1517 (2006).
37. H.-J. Lie, C.-H. Cho, J.-H. Lee, S. Lee, *J. Geophys. Res.* **108**, (C3), 3077 (2003).

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Time-Critical Social Mobilization

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The World Wide Web is commonly seen as a platform that can harness the collective abilities of large numbers of people to accomplish tasks with unprecedented speed, accuracy, and scale. To explore the Web's ability for social mobilization, the Defense Advanced Research Projects Agency (DARPA) held the DARPA Network Challenge, in which competing teams were asked to locate 10 red weather balloons placed at locations around the continental United States. Using a recursive incentive mechanism that both spread information about the task and incentivized individuals to act, our team was able to find all 10 balloons in less than 9 hours, thus winning the Challenge. We analyzed the theoretical and practical properties of this mechanism and compared it with other approaches.

In crowdsourcing, an interested party provides incentives for large groups of people to contribute to the completion of a task (1, 2). The nature of the tasks and the incentives vary substantially, ranging from monetary rewards, to entertainment, to social recognition (3–7).

A particularly challenging class of crowdsourcing problems requires not only the recruitment of a very large number of participants but also extremely fast execution. Tasks that require this kind of time-critical social mobilization include search-and-rescue operations, hunting down outlaws on the run, reacting to health threats that

need instant attention, and rallying supporters of a political cause.

To mobilize society, one may turn to mass media. However, the ability to use mass media can be inhibited for many reasons, such as telecommunications infrastructure breakdown. In such cases, one must resort to distributed modes of communication for information diffusion. For example, in the aftermath of Hurricane Katrina amateur radio volunteers helped relay 911 traffic for emergency dispatch services in areas with severe communication infrastructure damage (8). At other times, the nature of the task itself necessitates socially driven diffusion because it requires tight involvement that can only be generated socially.

Another common characteristic of these social mobilization problems is the presence of some sort of search process. For example, search may be conducted by members of the mobilized community for survivors after a natural disaster. Another kind of search attempts to identify indi-

viduals within the social network itself, such as finding a medical specialist to assist with a challenging injury.

There is growing literature on search in social networks. It has long been established that social networks are very effective at finding target individuals through short paths (9), and various explanations of this phenomenon have been given (10–13). However, the success of search in social mobilization requires individuals to be motivated to actually conduct the search and participate in the information diffusion; indeed, the majority of chains observed empirically terminate prematurely. Providing appropriate incentives is a key challenge in social mobilization (14, 15).

Recognizing the difficulty of time-critical social mobilization, the Defense Advanced Research Projects Agency (DARPA) announced the DARPA Network Challenge in October 2009. Through this challenge, DARPA aimed to “explore the roles the Internet and social networking play in the timely communication, wide-area team-building, and urgent mobilization required to solve broad-scope, time-critical problems” (16). The challenge was to provide coordinates of 10 red weather balloons placed at different locations in the continental United States. According to DARPA, “a senior analyst at the National Geospatial-Intelligence Agency characterized the problem as impossible” by conventional intelligence-gathering methods (17).

We, as the Massachusetts Institute of Technology (MIT) team, won the challenge (18), completing the task in 8 hours and 52 min. In ~36 hours before the beginning of the challenge, we were able to recruit almost 4400 individuals through a recursive incentive mechanism. Between

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50 and 100 other teams participated in the DARPA Network Challenge (17). Although no other team located the 10 balloons, The Georgia Institute of Technology (GaTech) team placed second by locating nine balloons within 9 hours. Two more teams found eight balloons (Dudeftsa-Balloon and Rodriguez-Chang), and five other teams found seven balloons. Variations in the strategies of the competing teams reflected differences in how social media can be tailored in order to fit a given task (19).

The MIT team’s strategy for public collaboration was to use the \$40,000 prize money that would be awarded to the winning team as a financial incentive structure rewarding not only the people who correctly located balloons but also those connecting the finder to us. Should we win, we would allocate \$4000 in prize money to each of the 10 balloons. We promised \$2000 per balloon to the first person to send in the correct balloon coordinates. We promised \$1000 to the person who invited that balloon finder onto the team, \$500 to whoever invited the inviter, \$250 to whoever invited that person, and so on. The underlying structure of the “recursive incentive” was that whenever a person received prize money for any reason, the person who invited them would also receive money equal to half that awarded to their invitee (fig. S1).

Our approach (“mechanism”) was based on the idea that achieving large-scale mobilization

requires incentives at the individual level to execute the task as well as to be actively involved in the further recruitment of other individuals through their social networks. A formal model of the approach is in the supporting online material (SOM) text. In this diffusion-based task environment, agents become aware of tasks as a result of either (i) being directly informed by the mechanism through advertising or (ii) being informed through recruitment by an acquaintance agent (20).

Our approach can be seen as a variant of the Query Incentive Network model of Kleinberg and Raghavan (21), in which a query propagates over a network through a subcontracting process, and the answer propagates back once it is found (SOM text). The use of incentives to spread information on a social network is also frequent in referral marketing programs, which encourage existing customers to promote the product among their peers—for example, by giving the customer a coupon for each friend recruited (22). A fundamental difference between these techniques and ours is that our reward scales with the size of the entire recruitment tree (because larger trees are more likely to succeed), rather than depending solely on the immediate recruited friends.

Our mechanism’s performance compares well with previous studies on search and recruitment in social networks. One measure of success is the size of the cascades, both in terms of number of nodes, as well as depth. In a study

of the spread of online newsletter subscriptions (23), in which individuals were rewarded for recommending the newsletter to their friends, the 7188 cascades varied in size between 2 and 146 nodes, with a maximum depth of eight steps, over a time span of 3 months. In our data, if we ignore the MIT root node there were 845 trees recruited within 3 days. Examples of these trees are shown in fig. S5. The largest tree contained 602 nodes, and the deepest tree was 14 levels deep. The distribution of tree/cascade depth is shown in Fig. 1A. Furthermore, a power-law distribution of tree/cascade size with exponent -1.96 , as predicted by models of information avalanches on sparse networks, is shown in Fig. 1B (24).

Previous empirical studies reported attrition rates, which measure the percentage of nodes that terminate the diffusion process. For example, in a study of e-mail–based global search for 18 target persons, attrition rate varied between 60 and 68% in 17 out of the 18 searches performed (15). In another study of the diffusion of online recommendations, an attrition rate of 91.21% was reported, despite providing incentives to participants by offering them a chance in a lottery (24). In the DARPA Network Challenge, if we ignore isolated single nodes our mechanism achieved a significantly lower attrition rate of 56%.

Another measure of performance for social mobilization processes is the branching factor (also known as the reproductive number), which

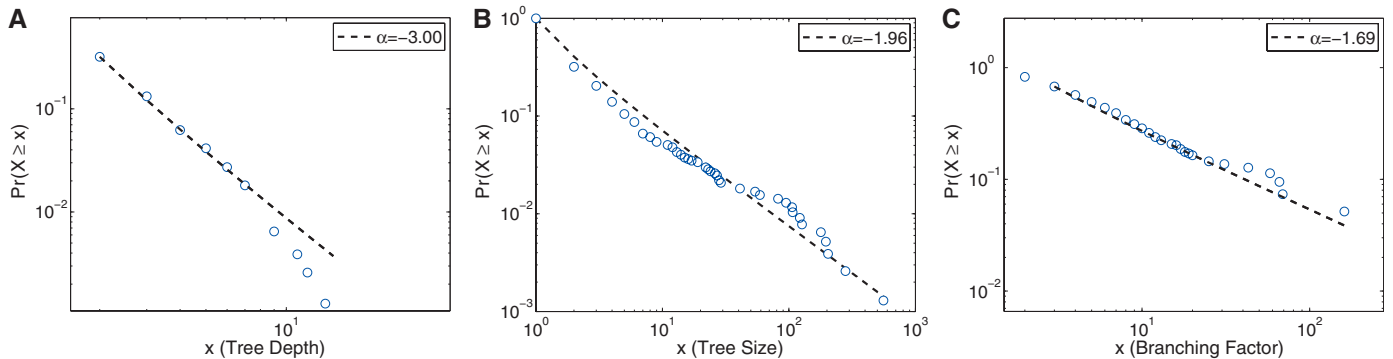


Fig. 1. (A) Distribution of tree depth on a log-log scale with a power law fit. (B) Distribution of tree size on a log-log scale with a power law fit. (C) Distribution of the branching factor on a log-log scale with a power law fit.

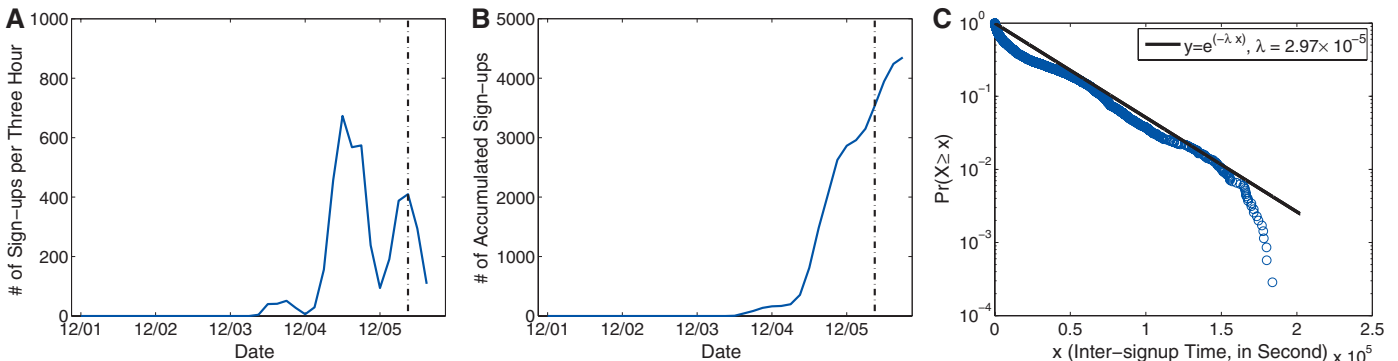


Fig. 2. (A) Number of people recruited over time up to the winner announcement. The dotted line indicates the time the balloons were launched into their positions by DARPA. (B) Cumulative number of people recruited over time. (C)

Complementary cumulative distribution of the inter–signup time on a semi-log scale with an exponential fit. Shown is a larger-than-exponential drop off at the end of the graph, which is due to the time-critical nature of the task.

is the number of people recruited by each individual. Previous empirical studies reported diverse, though mostly low, observations. In a study of the spread of support for online petitions, dissemination was very narrow, with >90% of nodes having exactly one child (25), which others have attributed to a selection bias, observing only large diffusions (26). In our data, the average branching factor was 0.93 if we exclude single-node trees (0.80 if we include single-node trees). The branching factor follows a power-law distribution, suggesting that certain individuals played an important role in dissemination by recruiting a very large number of people (Fig. 1C). Our data also compares very favorably with the newsletter subscription experiment mentioned above, in which spreaders invited an average of 2.96 individuals but were only able to cause 0.26 individuals to sign up on average (23). More generally, our data indicates that the branch-

ing factor appears to be closer to the tipping point (branching factor of 1), above which large cascades ensue. However, the cascade was finite because of the completion of the task.

The dynamics of recruitment over time are shown in Fig. 2, A and B, highlighting two bursts of day-time recruitment activities on Friday and Saturday just before DARPA launched the balloons into their locations. In contrast with the newsletter subscription experiment (23), in which diffusion experienced a continuous decay, these bursts enabled our mechanism to amass a large number of people quickly.

Moreover, in the newsletter subscription experiment the dynamics of diffusion were slow, which was attributed to a heterogeneous, non-Poisson distribution of individuals' response time. We observed an exponential distribution of inter-sign-up time (Fig. 2C) (27). This contrasts with the empirically observed power-law distribution

of inter-response time in human activity (28, 29) and information cascades (23).

In message-routing tasks, it has been argued that the ability of individuals to find a target with an approximately known location is largely attributed to people's ability to exploit geography (11, 15). To investigate this, we plotted the probabilistic density distribution of distances between two parties in a successful recruitment (Fig. 3). We compared this data with a best-fit model that explains the distribution of friendship over geographical distance in the popular LiveJournal online community (Fig. 3) (30). Our data exhibited higher likelihood of distant connections compared with the model by Liben-Nowell *et al.* (30). Furthermore, this was confirmed by applying the Kolmogorov-Smirnov test, comparing our data with random samples drawn from the model ($P < 10^{-100}$). This suggests that people may have exerted greater effort in recruiting distant friends. This might be due to an expectation that increasing the geographic spread of their recruitment sub-tree is likely to increase their expected reward.

Because the DARPA challenge was not designed specifically as an experiment, the potential for comparison with the other teams is limited. To provide a qualitative comparison of diffusion between the MIT team and other teams, we analyzed data from the information network Twitter. We obtained ~100 million tweets for the time period from 10 November to 9 December. This data set covers an estimated 20 to 30% of all public tweets for that period (31). Initially, we filtered out all tweets except those containing the string "balloon" in a case-insensitive manner. We analyzed five teams in the top 10 final standings with a Twitter presence: MIT, GaTech, Hotz, Geocatcher, and Deci/Nena, representing different strategy categories. We then kept track of the number of tweets that included either of the following as tweet content about the team: team name, team website, hashtag for the team, short link for the team Web site, and team's affiliation name, including the abbreviation. The tweet counts are shown in Fig. 4.

The GaTech team adopted an altruism-based incentive method, by offering to donate all proceeds to the American Red Cross. The limited number of tweets responding to their strategy suggests that relying purely on altruistic propagation is not sufficient to amass large social mobilization. Because of their early start, mass media coverage, and search engine optimization, they ended up locating nine balloons with 1400 active members, and ranked second in the final list (19).

Another class of strategies is those that capitalize on an existing community of interest to which a team had direct access. We refer to this as the community-based strategy. George Hotz is a Twitter celebrity with more than 35,000 followers, and his strategy was to use his fame on Twitter to solicit help. He successfully created a burst in Twitter on the day he announced his participation in the competition, and ended up finding eight balloons (four from his Twitter

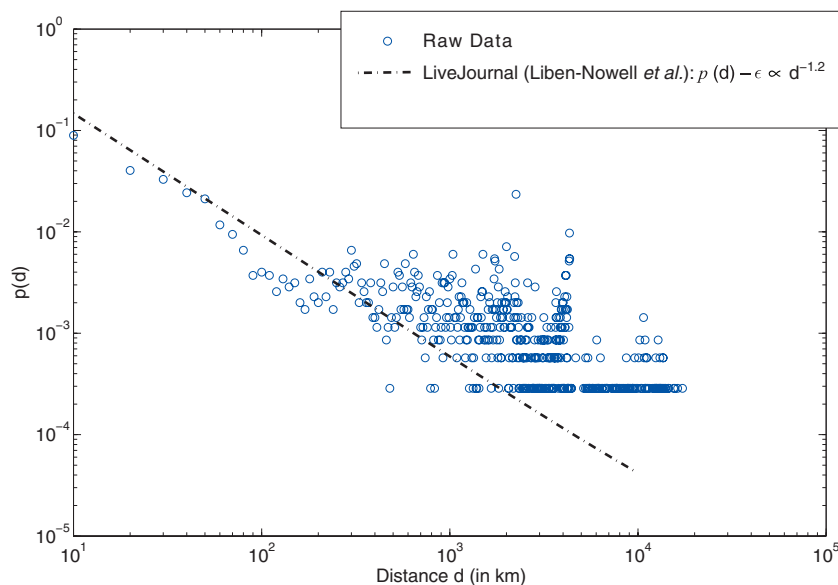


Fig. 3. Distribution of distance between recruiter nodes and their recruits. The dotted line shows the best-fit rank-based friendship model by Liben-Nowell *et al.* (30). We apply the same treatment to our data points as in Liben-Nowell *et al.* by rounding distances to multiples of 10 km. Approximate geographic locations were discovered from users' Internet provider addresses during sign-up.

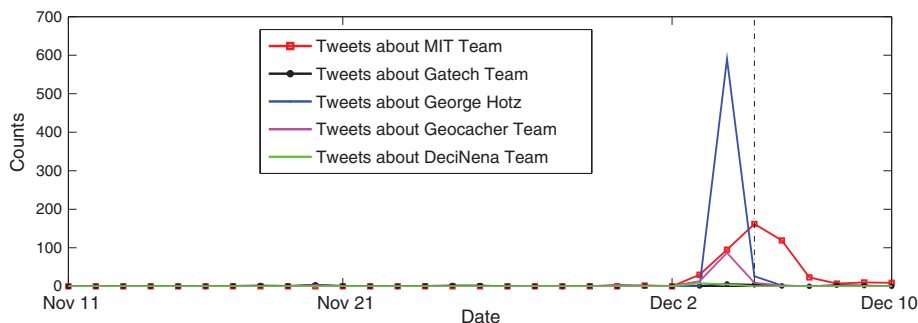


Fig. 4. Raw tweet counts for five teams from the announcement of the challenge to the announcement of the winner. The time series starts at the announcement of the challenge and ends at the announcement of the winner. The dotted line marks the time at which the balloons were launched. The MIT team launched its Web site and mechanism only 2 days before the balloon launch.

network, and four through trades with other teams) (17). Similarly, Geocacher's strategy was based on the existing community of geocaching, a sport based on using navigational techniques to hide and seek objects. It also created a burst by announcing its participation to the geocacher community and located seven correct balloons. DeciNena aimed at assembling a balloon-hunting team by posting their participation on every related blog on the Internet to gain attention, but they failed to achieve a wide-range response. DeciNena found seven balloons at the end of the competition.

Although Hotz and Geocacher were able to create a sudden response peak by efficiently propagating the news to an existing audience, this response was very short-lived. On the other hand, our strategy was able to sustain social response for a longer period, stretching up until the end of the competition. This happened despite not having access to a large community of followers. Instead, the MIT team started with only four people; and after a couple of days, twitter response achieved a number comparable with that of Hotz, who started with 35,000 existing followers. Another interesting observation is that after the competition, when mass media came to report the winning story of the MIT team the tweet count actually decreased instead of increasing. This suggests that the incentives provided by the MIT strategy played a dominant role in generating Twitter response, rather than the "MIT brand" and mass media effect (SOM text).

The recursive incentive mechanism has a number of desirable properties. First, the recursive incentive mechanism is never in deficit—it never exceeds its budget (SOM text). After being recruited by a friend, an individual has no incentive to create his own root node by visiting the Balloon Challenge Web page directly (without using the link provided by the recruiter). This follows from the fact that payment to the person finding the balloon does not depend on the length of the chain of recruiters leading to him.

However, the mechanism is not resistant to false name attacks, which were originally identified in the context of Web-based auctions (32). In this attack, which has been shown to plague powerful economic mechanisms (32), an individual creates multiple false identities in order to gain an unfair advantage. Having said that, our data does not reveal any successful incidents of false-name attacks. This may be due to the fact that the mechanism did not operate for long enough for people to identify this potential, and that actual payment requires social security numbers. In practice, other measures could be put in place to minimize or detect this kind of attack (33).

The mechanism's success can be attributed to its ability to provide incentives for individuals to both reports on found balloon locations while simultaneously participating in the dissemination of information about the cause. When an individual finds a balloon, the individual can either report the balloon to us, to other teams, or attempt to find the other nine balloons and win

the DARPA prize directly. In practice, it is unlikely for an unprepared individual to find other balloons (and if they replicated our mechanism, their delayed start would always leave them behind). Proofs are in the SOM.

Our mechanism simultaneously provides incentives for participation and for recruiting more individuals to the cause. This mechanism can be applied in very different contexts, such as social mobilization to fight world hunger, in games of cooperation and prediction, and for marketing campaigns.

References and Notes

- J. Howe, *Crowdsourcing: Why the Power of the Crowd Is Driving the Future of Business* (Three Rivers Press, New York, 2009).
- E. Hand, *Nature* **466**, 685 (2010).
- L. von Ahn, *Computer* **39**, 92 (2006).
- S. Cooper et al., *Nature* **466**, 756 (2010).
- J. Pontin, *New York Times*, Artificial intelligence, with help from the humans (25 March 2007); available at www.nytimes.com/2007/03/25/business/yourmoney/255stream.html.
- K. J. Arrow et al., *Science* **320**, 877 (2008).
- B. A. Huberman, D. M. Romero, F. Wu, *J. Inf. Sci.* **35**, 758 (2009).
- G. Krakow, "Ham radio operators to the rescue after Katrina: Amateur radio networks help victims of the hurricane," www.msnbc.msn.com/id/9228945 (2005).
- S. Milgram, *Psychol. Today* **1**, 6067 (1967).
- J. M. Kleinberg, *Nature* **406**, 845 (2000).
- D. J. Watts, P. S. Dodds, M. E. J. Newman, *Science* **296**, 1302 (2002).
- L. A. Adamic, E. Adar, *Soc. Networks* **27**, 187 (2005).
- M. Rosvall, P. Minnhagen, K. Sneppen, *Phys. Rev. E Stat. Nonlin. Soft Matter Phys.* **71**, 66111 (2005).
- P. S. Dodds, R. Muhamad, D. J. Watts, *Science* **301**, 827 (2003).
- W. Mason, D. J. Watts, *Proceedings of the ACM SIGKDD Workshop on Human Computation* (ACM, New York, 2009), pp. 77–85.
- Defense Advanced Research Projects Agency, DARPA Network Challenge (accessed May 2010); available at <http://networkchallenge.darpa.mil>.
- Defense Advanced Research Projects Agency, DARPA Network Challenge Project Report (February 16, 2010); available at www.hdsl.org/?view&did=17522.
- Defense Advanced Research Projects Agency, "MIT Red Balloon Team wins DARPA Network Challenge" (press release, 5 December 2009).
- J. C. Tang et al., *Commun. ACM* **54**, 78 (2010).
- D. J. Watts, J. Peretti, *Harv. Bus. Rev.* **May**, 22 (2007).
- J. Kleinberg, P. Raghavan, in *Proceedings of 46th Annual IEEE Symposium on FOCS* (IEEE, Los Alamitos, CA, 2005), pp. 132–141.
- E. Bjalogorsky, E. Gerstner, B. Libai, *Mark. Sci.* **20**, 82 (2001).
- J. Iribarren, E. Moro, *Phys. Rev. Lett.* **103**, 038702 (2009).
- D. J. Watts, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 5766 (2002).
- D. Liben-Nowell, J. Kleinberg, *Proc. Natl. Acad. Sci. U.S.A.* **105**, 4633 (2008).
- B. Golub, M. O. Jackson, *Proc. Natl. Acad. Sci. U.S.A.* **107**, 10833 (2010).
- Our data does not include the time stamp of sending out invitations, but we were able to measure the intervals between actual sign-up events between a parent and its children in the trees.
- A. L. Barabási, *Nature* **435**, 207 (2005).
- R. D. Malmgren, D. B. Stouffer, A. S. Campanharo, L. A. Amaral, *Science* **325**, 1696 (2009).
- D. Liben-Nowell, J. Novak, R. Kumar, P. Raghavan, A. Tomkins, *Proc. Natl. Acad. Sci. U.S.A.* **102**, 11623 (2005).
- J. Yang, J. Leskovec, *Proceedings of the 4th ACM International Conference on Web Search and Data Mining* (ACM, Kowloon, Hong Kong, 2011).
- M. Yokoo, Y. Sakurai, S. Matsubara, *Games Econ. Behav.* **46**, 174 (2004).
- D. Whitworth, Man fined over fake eBay auctions. *BBC Newsbeat* (5 July 2010); available at www.bbc.co.uk/newsbeat/10508913.

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The Complex Folding Network of Single Calmodulin Molecules

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Direct observation of the detailed conformational fluctuations of a single protein molecule en route to its folded state has so far been realized only in silico. We have used single-molecule force spectroscopy to study the folding transitions of single calmodulin molecules. High-resolution optical tweezers assays in combination with hidden Markov analysis reveal a complex network of on- and off-pathway intermediates. Cooperative and anticooperative interactions across domain boundaries can be observed directly. The folding network involves four intermediates. Two off-pathway intermediates exhibit non-native interdomain interactions and compete with the ultrafast productive folding pathway.

The energy landscape view provides a conceptual framework for understanding protein folding (1, 2). However, the diversity

in size and structure of the proteome is far too large to provide a single generic mechanism for how proteins fold. Deciphering specific mechanisms

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