

sume by extension that lentiviral vectors would be less prone to such a dramatic side effect because they avoid integrating their genomes close to promoters? It is true that MLV readily induces leukemia in mice, whereas no lentivirus has been observed to cause cancer (superinfection with other viruses and loss of immune surveillance, not HIV itself, are responsible for malignancies observed in AIDS). Nevertheless, other factors may be important. First, HIV and other lentiviruses usually infect terminally differentiated cells, that is, cells far less likely than immature progenitors to embark upon uncontrolled proliferation. Second, lentiviruses in general may be more cytopathic than oncoretroviruses, which implies that their target cells may rarely live long enough to become transformed. Still, and even though

some enhancers are capable of influencing promoters from great distances, the possibility that lentiviral vectors are less likely than their oncoretroviral counterparts to cause tumors by insertional mutagenesis calls for a careful comparison of their oncogenic potential in relevant animal models.

Notably, a degree of “transcriptional immunity” seems to protect integrated HIV vectors from their genomic environment, at least in some situations. The successful generation of transgenic animals by lentivector-mediated transduction of single-cell embryos or embryonic stem cells indicates that lentiviral vectors are not developmentally silenced (14). This sharply contrasts with oncoretroviruses, which in similar settings become potentially repressed by methylation-dependent and -independent epigenetic mechanisms (15).

Whether the avoidance of promoter regions or some other cis-acting phenomenon explains the ability of lentiviral vectors to resist these negative influences is only one of many exciting questions raised by the Wu *et al.* study.

References

1. J. Coffin, H. Varmus, S. Hughes, Eds. *Retroviruses* (Cold Spring Harbor Press, Cold Spring Harbor, NY, 2000).
2. A. R. W. Schroder *et al.*, *Cell* **110**, 521 (2002).
3. X. Wu *et al.*, *Science* **300**, 1749 (2003).
4. U. Greber, A. Fassati, *Traffic* **4**, 136 (2003).
5. M. Bukrinsky *et al.*, *Nature* **365**, 666 (1993).
6. N. K. Heinzinger *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **91**, 7311 (1994).
7. A. Fassati, S. P. Goff, *J. Virol.* **73**, 8919 (1999).
8. L. Li *et al.*, *J. Virol.* **74**, 10965 (2000).
9. L. Li *et al.*, *EMBO J.* **20**, 3272 (2001).
10. C.-W. Lin, A. Engleman, *J. Virol.* **77**, 5030 (2003).
11. G. V. Kalpana *et al.*, *Science* **266**, 2002 (1994).
12. A. Hacein-Bey *et al.*, *N. Engl. J. Med.* **348**, 255 (2003).
13. A. Fischer *et al.*, personal communication.
14. C. Lois *et al.*, *Science* **295**, 868 (2002).
15. S. R. Cherry *et al.*, *Mol. Cell. Biol.* **20**, 7419 (2000).

PHYSICS

How to Freeze Out Collisions

Massimo Inguscio

In an atomic “clock,” an oscillator is locked to a well-defined and reproducible atomic resonance frequency, allowing time to be measured with extraordinary precision and accuracy. Ultracold atoms provide particularly accurate clocks because they move extremely slowly, reducing errors and uncertainties associated with motion. The realization of Bose-Einstein condensates—dilute atomic samples at nanokelvin temperatures (1)—may enable further improvements in precision time measurements.

However, atomic interactions may shift the atomic energy levels, limiting the accuracy of atomic clocks made with Bose-Einstein condensates (2, 3). At ultralow temperatures, atoms can only collide head-on. Because the Pauli exclusion principle prevents two indistinguishable fermions from being in the same state at the same time, indistinguishable fermions cannot collide. Therefore, fermion atoms may provide clock transitions that exhibit no collisional shift, providing an intriguing alternative (2) to bosonic atoms.

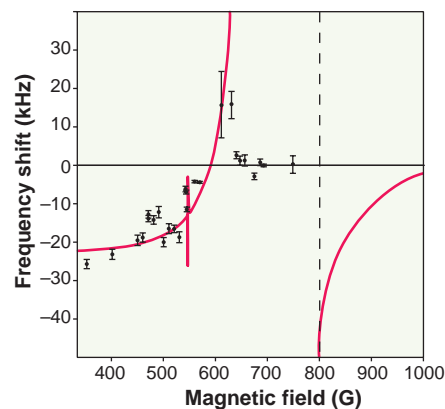
On page 1723 of this issue (4), Gupta *et al.* realize such a fermion clock transition without collisional shifts. In their experiment, (fermionic) ${}^6\text{Li}$ gas is cooled to a few microkelvins with the help of (bosonic)

sodium. An infrared laser beam then traps the ${}^6\text{Li}$ atoms in the lowest energy levels (see the first figure). Starting with all atoms either in state 1 or 2, Gupta *et al.* show that the radio-frequency clock transition (see first figure) is not affected by collisions (4).

Because of radio-frequency transfer from one level to the other, atoms should no longer be indistinguishable, because they occupy two different “spin” states. Hence collisions should take place. Yet, the authors argue that interaction with the radio-frequency radiation induces a coherent superposition of the two different spin states and hence the atoms remain, at least for a while, indistinguishable and no collisional shift takes place. Only after the coherence of the superposition state is lost, with the subsequent formation of a

pure statistical mixture of the two states, collisional shifts are again observed.

When collisions affect two atomic levels in a different way, the relevant transition frequency can be changed dramatically. In the optical domain such an effect has been crucial for obtaining a signature of a hydrogen Bose-Einstein condensate (5). Important changes in the collisional perturbation of an atomic level can be induced by resonances (6, 7), which occur when the collision energy of two free atoms coincides with that of a quasi-bound molecular state between the two free atoms. In such scattering resonances, produced by means of an external magnetic field, the scattering length can be tuned from large positive (re-

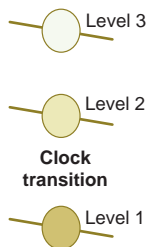


Radio-frequency probe of atomic interactions. A resonance between atoms in levels 2 and 1 is induced by an external magnetic field. The perturbation of 2 is probed through the shift of the 2 → 3 radio-frequency transition. The red curve is the shift as evaluated from the scattering length. The dashed line indicates the position of the Feshbach resonance measured in (9).

pulsion) to large negative (attraction) values.

Radio-frequency spectroscopy allows this behavior of ultracold atoms to be monitored, as shown by Gupta *et al.* for ${}^6\text{Li}$ (4) and, independently, by Regal and Jin for ${}^{40}\text{K}$ (8). The magnitude and sign of the frequency shift of a transition involving a level affected by a Feshbach resonance turn out to depend on the magnitude and sign of the scattering length (see the second figure).

In the experiment of Gupta *et al.*, very small shifts are observed for magnetic fields above 630 G where instead a Feshbach resonance recently measured around 800 G by Bourdel *et al.* (9) should lead to a huge shift. These deviations from the expected behavior indicate that something new is happening. When the scattering length becomes comparable with the interatomic spacing, the scattering cross section reaches its maximum



The lowest levels of ${}^6\text{Li}$ separated by radio-frequency transitions. The transition from level 1 to 2 is used in (4) to realize a “clock” transition void of collisional shifts.

The author is in the Department of Physics, LENS, and INFN, University of Florence, 50019 Florence, Italy. E-mail: inguscio@lens.unifi.it

and no longer depends on the scattering length. This is known as the unitarity limit regime. The quenching of the shift in the lithium spectrum measured by Gupta *et al.* could be related to this phenomenon. Regal and Jin have reported a similar saturation in the radio-frequency reconstruction of Feshbach resonances in potassium. Radio-frequency techniques certainly provide additional insights into this puzzling behavior of strongly interacting Fermi systems (10).

The Feshbach resonance at 800 G between the two lowest states of ${}^6\text{Li}$ has been used by O'Hara *et al.* (11) to create a strongly interacting Fermi gas. Their observation of an anisotropic expansion following a sudden release of the gas did not, however, provide unambiguous evidence for a Fermi superfluid. Anisotropic expansion can arise not only from superfluidity but also from strong collisional effects. Regal *et al.* and Bourdel *et al.* (9) have shown, respectively, for fermionic potassium and lithium, that a strongly interacting lithium Fermi gas that is not yet in the superfluid phase can indeed expand anisotropically. The precise radio-frequency control of interac-

tions around a Feshbach resonance may help in characterizing superfluid features also for strongly interacting fermionic potassium (8).

Radio-frequency spectroscopy was invented by Fermi and Rasetti as a tool for investigating atomic spectra (12). Nearly 80 years later, the same technique is used to characterize intriguing effects associated with the Fermi quantum statistics. Through its application to degenerate Fermi gases, radio-frequency spectroscopy allows interactions between fermions to be probed with unprecedented accuracy, particularly in regimes where universal laws and fascinating phenomena such as superfluidity may be explored.

Further important developments are ahead of us. Ramping a magnetic field through a Feshbach resonance has been used as one of the ways to couple bosonic atoms into molecules. Fermionic atoms appear to be better candidates. Ultracold molecules have been created by means of a Feshbach resonance in a degenerate fermion potassium gas (13). Radio-frequency spectroscopy turns out to be important in detecting photodissociation spectra of the weakly bound molecules.

With the production of ultracold molecules, also speculated for ${}^6\text{Li}$ (9, 14) exciting developments are inevitable. Also, heteronuclear dimers may be formed out of atomic mixtures (15). In this emerging new scenario, radio-frequency spectroscopy will certainly play a crucial role in deepening our understanding of matter at such ultralow temperatures.

References

1. M. Inguscio *et al.*, Eds., *Proc. Int. School of Physics "E. Fermi", Course CXL* (IOS Press, Amsterdam, 1999).
2. D. M. Harber *et al.*, *Phys. Rev. A* **66**, 053616 (2002).
3. A. Gorlitz *et al.*, *Phys. Rev. Lett.* **90**, 090401 (2003).
4. S. Gupta *et al.*, *Science* **300**, 1723 (2003); published online 8 May 2003 (10.1126/science.1085335).
5. T. C. Killian *et al.*, *Phys. Rev. Lett.* **81**, 3807 (1998).
6. U. Fano, *Nuovo Cimento* **12**, 156 (1935).
7. H. Feshbach, *Ann. Phys. (N.Y.)* **5**, 357 (1958).
8. C. A. Regal, D. S. Jin, <http://arxiv.org/abs/condmat/0302246>.
9. T. Bourdel *et al.*, <http://arxiv.org/abs/cond-mat/0303079>.
10. L. Pitaevskii, S. Stringari, *Science* **298**, 2144 (2002).
11. K. M. O'Hara *et al.*, *Science* **298**, 2179 (2002).
12. E. Fermi, F. Rasetti, *Nature* **115**, 764 (1925).
13. C. A. Regal *et al.*, <http://arxiv.org/abs/cond-mat/0305028>.
14. S. Kokkelmans, invited talk S3.001 at the 34th DAMOP conference, 20 to 24 May 2003, Boulder, CO.
15. A. Simoni *et al.*, *Phys. Rev. Lett.* **90**, 163202 (2003).

PSYCHOLOGY AND ECONOMICS

Strategizing in the Brain

Colin F. Camerer

Most economic theories minimize the influence of human emotions and assume that what people believe and choose follows rationality principles. Important principles include knowing how much of one valuable good is worth one unit of another; following the rules of probability in processing information; planning

Enhanced online at
www.sciencemag.org/cgi/content/full/300/5626/1673

ahead; resisting temptation; and guessing accurately what others will do. These principles have proved useful as mathematical building blocks for devising aggregate theories of corporate and market behavior. An emerging field of study called "behavioral economics" takes advantage of dramatic advances in psychology and neuroscience. Behavioral economics replaces strong rationality assumptions with more realistic ones and explores their implications (1). A clear demonstration of how neural evidence contributes to behavioral economics is provided by Sanfey *et al.* on page 1755 of this issue (2). These investigators analyzed subjects with functional magnetic resonance imaging as they played the "ultimatum game,"

and correlated activity in certain brain areas with the cognitive and emotional processes involved in economic decision-making.

In their version of the ultimatum (or "take-it-or-leave-it") game, a proposer offers a division of \$10 to a responder, who accepts it (ending the game) or rejects it, leaving both players with nothing. The prediction is that responders who want to earn the most money will take any offer; a self-interested proposer who anticipates this will offer the smallest amount. However, this prediction turns out to be wrong (offers are typically around 50% of the total amount, and 50% of low offers are rejected). Functional magnetic resonance imaging shows why. Subjects whose brains were imaged while they were presented with an unfair offer (\$1 to \$2 out of the \$10 available) showed greater activity in the bilateral anterior insula of the brain, revealing that such an offer created negative emotions. Those subjects with the strongest activation of the anterior insula rejected a higher proportion of unfair offers. The anterior cingulate (ACC), a brain region that detects cognitive conflict, also showed greater activity during presentation of an unfair offer, suggesting that this area mediates the conflict between earning money and feeling bad. These findings emphasize the importance of emotional influences in human decision-making.

In games like ultimatum bargaining, "players" with information choose "strategies" that, collectively, create outcomes that players like or dislike and to which they attach numerical valuations ("utilities"). Game theory can link economics to other sciences because it uses the same tools to model interactions at many different scientific levels (genes, firms, nation-states). But doing so requires extending the central assumptions of rational game theory, namely, that players are (i) self-interested and (ii) reach an "equilibrium" in which everyone is choosing (or planning) strategies that yield the best outcome, anticipating that others are doing the same. An emerging approach called "behavioral game theory" replaces these assumptions with precise alternatives that are more cognitively plausible (3).

One ingredient of behavioral game theory is a model of "social utility," showing how players' utilities for payoff allocations depend on how much others get, as well as on their own payoffs. This old idea is illustrated by many experiments showing that people routinely cooperate in the "prisoner's dilemma" game, in which "defection" is always better for one player but mutual "cooperation" makes everyone in a group better off. Prisoner's dilemma cooperation is well established, but evidence from newer games (like ultimatum bargaining) help to calibrate precise social utility functions that make fresh predictions (4).

One new game is "trust." In a trust game, one player can invest money that is multiplied (say, by 3) to reflect the investment's productivity. A second trustee player can repay or keep as much of the tripled investment as he

The author is in the Division of Humanities and Social Sciences 228-77, California Institute of Technology, Pasadena, CA 91125, USA. E-mail: camerer@hss.caltech.edu