plasticity to achieve a sophisticated series of structural and dynamical transitions. For According to this view, for each state along the enzymatic cycle of dihydrofolate reductase (DHFR) (*14*), a binding event can cause a protein molecule to occupy a new free-energy minimum (see the figure), stabilized by a ligand and geared to fluctuate toward another state that binds the next ligand in the catalytic cycle. The five successive steps of such transitions that exist in DHFR would thus show just how Five successive steps of such transitions exist in DHFR, showing just how effectively evolution can coordinate the thermal motion of hundreds of atoms to perform biological functions.

If this view turns out to be correct, then the free energy landscapes of enzymes are not just be simple funnelsThe free-energy landscapes of enzymes are thus not just simple funnels; rather, they form channels containing several low energy states. In the case of catalytic cycles, these free-energy channels are merged into rings that resemble rather battered sombreros (see the figure). Such a shape is created by stringing together several free-energy funnels, one for each of the structurally quite similar states along the catalytic cycle. The alignment of these funnels could results in a channeling mechanism that generates the complex motions required for enzymatic activity by breaking them down into simpler ones that are closely coupled to each other.

This Although much remains to be learned, this free-energy channel model mayis likely to be the result of a general type of free-energy surface that characterized by statistical pathways that enable the performance and regulation of catalytic reactions by a succession of binding events. Increasingly complex reactions couldcan be realized by generating further funnels along the channel. These Exploration of these concepts will beare particularly relevant in view of the increasing realization that enzymes—and other proteins—act as part of complex networks of interconnected processes.

Boehr *et al.* infer the structural similarity of an excited state with the ground state of the following step of the enzymatic cycle from the correlations between the chemical shifts of these states. Recent advances in protein structure determination (*5, 15*) using the same sort of nuclear magnetic resonance data that can be extracted from the type of experiments carried out by Boehr *et al.*, suggest that detailed structures of the excited states themselves could be just around the corner. Examination of such structures would undoubtedly enable these interesting concepts to be tested further. It could also Knowledge of such structures would further our understanding of the way proteins have evolved, would shed light on the role of the multiple protein-protein interactions now being discovered through proteomic techniques, and may be of great practical value for rational drug design.

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PHYSICS

Detecting and Controlling Electron Correlations

Measurement and control of fluctuations in circuits may lead to devices for quantum computation.

Markus Büttiker

As electronic devices shrink to nanometer dimensions, their properties are increasingly governed by quantum effects rather than classical physics. Electron motion is no longer a simple matter of electrical currents flowing in circuits, but is instead highly influenced by the diffraction and interference of the particle wave functions as described by quantum mechanics. In this case, the fluctuations exhibited by electron currents may contain information that is fundamental to understanding physics at nanometer scales. The ways in which such fluctuations are correlated in a nanostructure are interesting, especially for the possible construction of quantum information-processing elements. A recent experiment by Oberholzer *et al.* (*1*) shows how the quantum correlations between current fluctuations at two contacts of a normal conductor can be controlled simply by tuning an electrode voltage.

The physics of current fluctuations has been the subject of much experimental and theoretical exploration. The findings of Oberholzer *et al.* in particular confirm a theoretical prediction about current correlations made by Texier and Büttiker in 2000 (*2*). Previously, the sign of the current-current correlation measured between contacts in a device has always been connected to the statistical properties of the carriers (*3*). Electrons are fermions and the Pauli principle dictates that each state can only be singly occupied; as a consequence, current-current correlations in normal conductors are negative. Conversely, for current carriers that obey Bose-Einstein statistics (in which a given state can be occupied by multiple quanta), positive correlations are observed. To reverse the sign of these correlations, the experiment brings another effect into play: Electrons are carriers with charge. A charge imbalance leads to an electric field that in turn acts on all electrons in the same way within its range, leading to additional correlations. These correlations can dominate the antibunching effect of the Pauli principle and lead to positive correlations even in a purely normal conductor.

The geometry analyzed theoretically (*2*) and used in the experiment (*1*) is shown in the figure. The conductor consists of a high-mobility two-dimensional electron gas with a

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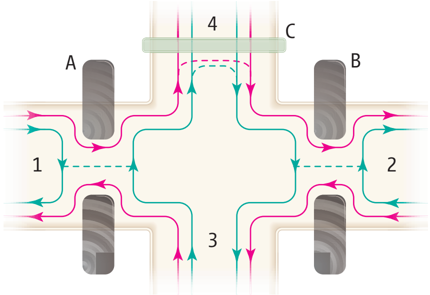
geometry determined by top gates (A, B, C in the figure). If a voltage is applied to the gates, they deplete the electron gas underneath them, thus generating the desired geometry. The conductor consists of two narrow orifices called quantum point contacts (QPCs), labeled A and B. Electron current is incident at contact 1, and the current correlations are measured between contacts 2 and 3. In addition, there is a fourth contact, which can be opened or closed with the help of a side gate C. The conductor is subject to a high magnetic field such that it is in an integer quantum Hall state. This allows the creation of states in which carriers skip in one direction along the edges ("edge states") that form the equivalent of controlled electron "beams," like the beams in an interferometer. The experiment is carried out for a magnetic field for which there are only two edge states. The two edge states are depicted in the figure with fine blue and green lines.

At low temperatures, if scattering events are purely elastic, noise is generated whenever there exists more than one final state for a given initial state. In the experiment, noise is generated at QPC A by adjusting the gates such that the inner edge state is only partially transmitted. A carrier incident in this state is reflected with some probability back into contact 1 or transmitted with some probability into contact 4 (if the gate to this contact is open). Therefore, this process creates an inner edge state leading away from the QPC with a carrier population that fluctuates in time. In contrast, the outer edge state transmits perfectly through the QPC and is noiseless.

If the gate at contact 4 is closed, both the outer noiseless edge state and the inner edge state approach the second QPC (denoted B in the figure). If QPC B is configured such that the noiseless edge state is fully transmitted and the inner edge state is fully reflected, then the current at contact 2 is noiseless, and its correlation with current at contact 3 is zero. If the QPC B is opened a bit such that the noisy edge state is partially transmitted, then both the current in contact 2 and that in contact 3 will fluctuate. The Pauli principle is dominant, and the correlation is negative. In fact, this configuration was examined in an earlier experiment by the same group (*4*) to demonstrate negative correlations (*4*–*6*). With both QPCs partially transmitting an edge state, the role of the first contact is simply to regulate the occupation of the edge state incident on the second QPC. If the transmission through QPC A is reduced, the population of the noisy edge state is more and more diluted and, consequently, the negative correlation becomes smaller and smaller.

The crucial addition in the new experiment is the fourth contact. It comes into play when the gate C to this contact is opened. The fourth contact is now not simply a current sink but a voltage probe. Ideally a voltage probe draws no net current. Because the current incident on the probe is noisy, the voltage in this contact must fluctuate. The fluctuating voltage acts on all carriers in the probe equally, and therefore it will reemit carriers in the two outgoing edge states in synchronism. If the QPC B is now set to reflect the inner edge state completely, even the outer fully transmitted edge state is noisy. The collective response due to the fluctuating voltage of the probe leads to positive correlations, as predicted (*2*) and observed in the experiment of Oberholzer *et al.* (*1*). Note that there is no violation of the Pauli principle: Both edge states emerging from the voltage probe remain at all times singly occupied.



An electron beam splitter. Experimental configuration for the detection of negative, zero, or positive current correlations.

The collective emission of carriers described here is not the only effect that can generate positive correlations in electrical conductors. Emission of a Cooper pair from a superconductor into the normal metal leads to a pair of electrons that can generate positive correlations (*7*, *8*). Similarly, normal conductors with ferromagnetic contacts can show positive correlations due to "spin" bunching or dynamical spin blockade (*9*, *10*). It is also known that high-frequency current correlations can be positive in purely normal conductors due to collective voltage fluctuations (*11*). Yet, the experiment by Oberholzer *et al.* (*1*) is the first one to report positive fluctuations. Moreover, in this experiment, the sign of the correlations can be changed simply by turning on and off a gate voltage (the connection to the voltage probe).

The collective emission of carriers from a voltage probe is at its core a classical effect. It is only the noise of the incident channel that is generated quantum mechanically (through transmission and reflection at QPC A). One might therefore ask whether there are other geometries that will also show positive correlations in normal conductors. The answer is yes: Wu and Yip (*12*) analyzed geometries in which a quantum coherent conductor is connected to macroscopic resistors at its contacts. As in the effect described above, voltage fluctuations at the connection of the mesoscopic conductor and the macroscopic classical resistors generate a feedback effect (a collective response) that leads to positive correlations. Still another set of geometries have been investigated by Rychkov and Büttiker (*13*): If noise is fed into a conductor that is made to behave classically through increased inelastic scattering, the current correlations are predicted to become positive. This leads to a picture in which a quantum coherent conductor exhibits negative correlations but a macroscopic conductor divides the incident noise in a collective manner and as a result exhibits positive correlations. A recent experiment by Chen and Webb (*14*) in which a noise source feeds current fluctuations into a beam splitter confirms this picture. And recently, McClure *et al.* (*15*) have demonstrated that the sign of current correlations of two capacitively coupled quantum dots can be changed simply by tuning gate voltages.

There is much interest in generating, manipulating, and detecting entangled states in electrical conductors. Of particular interest are proposals for accomplishing this with purely normal conductors (*16*). My colleagues and I have also made predictions that link entanglement to a two-particle Aharonov-Bohm effect in which no individual particle encircles the flux but two-particle states are sensitive to the flux (*17*). Observation of such quasiparticle entanglement requires that voltage fluctuations that generate collective effects are largely absent. Experiments such as those carried out by Oberholzer *et al.* will help us to understand the necessary conditions.

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