involved. One possibility is that to attain optimal binding between lysin and the receptor several amino acid changes are required in lysin when one change occurs in the receptor. This problem will probably be resolved if the three-dimensional structure of the egg receptor is clarified.

The molecular study of speciation has just begun. Although it has given us a glimpse into the complex nature of gene interactions in the evolution of reproductive isolation, most problems remain untouched (*8*). As molecular biologists foray into this area, more surprising properties of gene interactions may be revealed.

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PERSPECTIVES: QUANTUM DOTS

Controlling Artificial Atoms

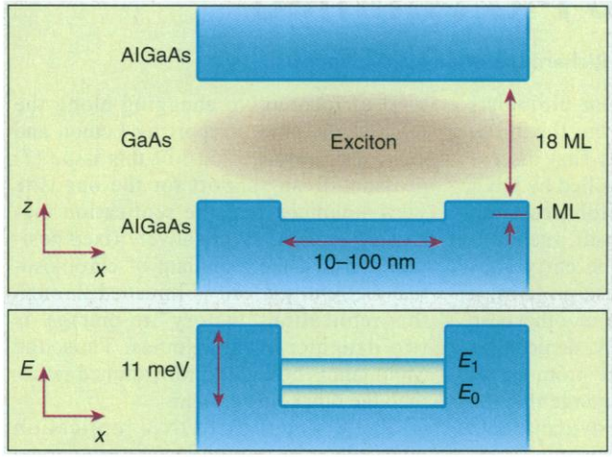
François H. Julien and Antigoni Alexandrou

Semiconductor quantum dots are fascinating objects. They contain up to a few hundred thousand atoms yet behave in many ways like one single gigantic atom. Their unique optical and transport properties are just being explored, but they already offer great promise for the development of extremely low threshold laser diodes, single-electron logic devices, or optical computing quantum units. As reported on page 1473 of this issue, Bonadeo *et al.* (*1*) have now achieved a remarkable degree of control of the quantum states of individual "artificial atoms."

Enhanced online at www.sciencemag.org/cgi/content/full/282/5393/1429

Quantum dots can be fabricated by colloidal chemistry techniques; by patterning, etching, electrostatic confinement, or monolayer fluctuations in thin semiconductor layers; and by controlling self-ordering mechanisms during epitaxial growth of strained semiconductor films (*2*). Although much progress has been made toward achieving large densities of uniform dots, the size fluctuations usually lead to an inhomogeneous broadening of the spectral features when observations are performed on an ensemble of dots. Some optical or transport properties associated with a single quantum dot have been reported by the use of nanoluminescence techniques or by fabricating single-electron transistors. This includes observations of extremely sharp luminescence lines (*3*), Coulomb-blockade effects in the one-by-one electron charging of the dots (*4*), or the Kondo effect (*5*). Bonadeo *et al.* (*1*) have achieved even deeper insight into the atomlike nature of semiconductor quantum dots by demonstrating the manipulation of the confined state wave functions of a single dot.

The quantum dots investigated in their study are formed by thickness fluctuations in a quantum well made of a thin layer of GaAs embedded in AlGaAs (*6*). If the quantum well is sufficiently thin (10 nm or less), a single monolayer increase of the well thickness causes large changes in confinement energy, and excitons can be localized in the three directions of space instead of just one in a perfectly flat interface quantum well. The formation of single-monolayer–high islands with lateral dimensions of 10 to 100 nm is achieved through epitaxial growth interruption by allowing surface migration of the atoms to their lower energy position at island edges. The size and shape are not really controlled, but the islands tend to be elongated and aligned along the [$\bar{1}$10] crystal axis. The interface quality is excellent, and extremely sharp lines have been observed by exciting and detecting the dot luminescence through micrometer-sized apertures in an aluminum mask. This masking technique allows selection of a few quantum dots within the broad distribution of dots. By combining spatial and spectral resolutions, it becomes possible to excite and probe only one individual quantum dot.



Artificial atom. (Top) A schematic diagram of a semiconductor quantum dot formed by a one-monolayer (ML)–high island in a narrow GaAs quantum well. **(Bottom)** The resulting energy diagram of the dot. Excitons are formed by the Coulombic interaction between one electron and one hole. They are analogous to a gigantic hydrogenic system with spatial extension on the order of tens of nanometers. One exciton can be trapped in the dot by the lateral confinement potential created by the monolayer-high island.

Bonadeo *et al.* (*1*) used a sequence of two laser pulses with a stabilized phase difference to coherently control the excitation state of these quantum dots. The interaction of light with a semiconductor creates a polarization in the material with a phase related to the phase of the exciting laser field. As long as this phase relation is preserved, the system is referred to as coherent. If a second pulse arrives with a well-defined phase difference (that is, a time delay τ) with respect to the first pulse, it generates a polarization that will interfere with the polarization created by the first pulse. Controlling the phase difference between the two pulses results in control of the interference between the two polarizations and thus control of the excitation state (namely, the wave function) of the system, hence the term coherent control. Although coherent control was first implemented in atomic and molecular physics, its application in semiconductor physics is very promising. A very simple demonstration of coherent control involving a single pulse was provided by the emission of terahertz (*7*) and midinfrared (*8*) radiation from semiconductor quantum wells: A broadband femtosecond pulse creates a coherent superposition of two states that results in a coherent charge oscillation emitting radiation at the difference fre-

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quency of the two states. In this case, the emission persists as long as the phase relation between the two excited states is preserved.

In real systems, however, coherence is lost because of processes such as collisions between electrons and interaction with lattice vibrations with a characteristic dephasing time. The important difference between previous coherent population control experiments in semiconductors (*9*) and the experiments presented by Bonadeo *et al.* (*1*) is that the dephasing time is much longer in a single dot (40 ps) than in bulk semiconductors (< 1 ps). The consequence is that a practically complete destruction of the population created by the first pulse is possible in a single quantum dot, whereas a destruction no better than 70% was achievable in the bulk material (*9*).

The feasibility of coherent control in a single quantum dot opens new perspectives for the use of quantum dots as quantum logic units for optical computing. Indeed, coherent control can be used to prepare the quantum dot in a target wave function that can be addressed optically. Multistate logic units could be achieved by the use of more than two confined states. Recent advances in quantum computation theory show that a chain of such quantum logic gates could perform sophisticated quantum computing operations such as factorization of large integer numbers in a much more efficient way than conventional two-state logic computers (*10*). The challenge now faced by scientists is to develop coherent control schemes useful for such applications. Moreover, one prerequisite for a practical quantum logic gate is a long decoherence time. In atoms, decoherence times as long as a few microseconds have been observed (*10*). Quantum dots, being solid-state systems, are technologically more practical than atoms, but much longer dephasing times still have to be achieved.

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PERSPECTIVES: DNA REPLICATION

Bringing the Mountain to Mohammed

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All too often, molecular biologists have underestimated the flexibility of DNA. When it was first discovered that genes can be controlled by DNA elements located many kilobases away from the transcribed gene itself, such "enhancers" were thought to be entry sites for regulatory proteins. These proteins, it was imagined, would slide or otherwise send a signal down the DNA, depicted as a static and rigid rod, to the promoter of the gene. Only later did it emerge that the DNA, which is of course dynamic and flexible, forms a loop that directly juxtaposes enhancer-bound regulatory proteins with the promoter-bound transcription complex. Similarly, until recently, textbooks depicted the replication fork for DNA duplication with two DNA polymerases independently carrying out leading-strand and lagging-strand synthesis. Now we know that the two polymerases are locked together in a rigid replication machine and that the DNA template for the lagging strand loops out from the twin polymerases. Because of the enormous length of DNA, textbooks have also generally depicted the chromosome as stationary and the replication machinery as a kind of locomotive chugging along the DNA track. Now a report by Lemon and Grossman on page 1516 of this issue (*1*) provides fresh support for the opposite view—namely, that the replication machinery remains at a relatively fixed position and that the mountain of chromosomal DNA in the cell is threaded through this replication "factory" to emerge as two daughter chromosomes. Thus, the Mountain is brought to Mohammed rather than the other way around.

The concept that DNA replication takes place in immobile factories arose from four sets of experiments in eukaryotic cells (*2*). First, eukaryotic chromosomes have multiple origins of replication, and evidence showed that these origins often fire synchronously, as if the initiation of replication was somehow coordinated among origins that were widely spaced along the chromosome (*3*). Second, direct visualization by fluorescence microscopy revealed that replication is initiated at a relatively small number of discrete sites within the nucleus at which many origins are clustered (*4*). Third, these sites were shown to contain the protein machinery for DNA replication (*2*). Finally, and most telling, time-lapse experiments with pulse-labeled DNA revealed a punctate pattern of DNA synthesis in the nucleus and the extrusion of newly duplicated DNA from the sites of replication (*5*). Apparently, DNA is spooled through stationary replication factories during the process of DNA duplication. Berezney and colleagues (*6*) have recently extended this analysis to demonstrate the existence of distinct factories for transcription as well as replication, the subject of a recent Perspective by Cook (*6*).

A formidable challenge to proving that DNA is indeed threaded through immobile replication factories is the immense complexity of the process of DNA duplication in eukaryotic cells. During the S phase of the cell cycle, the nucleus contains more than 100 putative factories, and each factory contains as many as 300 replication forks (*3*). Hence, it is difficult to determine the position of individual factories relative to the architecture of the nucleus and therefore to be certain that the factories remain stationary and that DNA is spooled through them. Confidence in the factory model would be much higher if it were possible to visualize single replication forks and to monitor their location relative to cellular landmarks. Now Lemon and Grossman (*1*) have done just that through their discovery of what appears to be replication factories in the bacterium *Bacillus subtilis*.

Bacteria, which lack nuclei, have traditionally been viewed as vessels with proteins diffusing freely within an amorphous cytoplasm. Recent applications of electron and fluorescence microscopy, however, have revealed that many proteins in bacteria have distinct subcellular addresses (*7*). Furthermore, the prokaryotic chromosome is oriented in a specific way in bacteria, and bacteria may have a "mitotic apparatus" that is responsible for chromosome segregation during the

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