tions during crystallization. This was unexpected, because the isolated Bateman domains from the mammalian γ subunits bind two molecules of AMP or ATP (*3*). This is likely to be a genuine difference between the mammalian and yeast enzymes.

In the new structures, a positively charged side chain in domain B (lowest "+" symbol in the figure) interacts with negatively charged phosphate(s) on AMP or ATP. A mutation of the equivalent side chain in the human enzyme (γ2 variant) that causes severe heart disease also greatly reduces binding of AMP (*10*). In the human enzyme, mutations in positively charged side chains occupying similar positions in CBS1 and CBS2 (upper "+" symbols in the figure) cause similar effects (*3*), supporting the idea that domain A also binds AMP in humans. Recently, my laboratory has provided evidence for a mechanism of activation of the human enzyme by AMP (*11*) that involves binding of AMP to these side chains. These residues are not conserved in the fission or budding yeast enzymes, which might explain why the latter is not activated by AMP.

Resolving these remaining uncertainties and anomalies will require structures of mammalian complexes in the presence of AMP or ATP, together with other methods to study domain interactions, especially of those domains not present in the structures reported by Townley and Shapiro. The effort will be very worthwhile if it facilitates development of new drugs aimed at treatment of the epidemic of obesity and diabetes.

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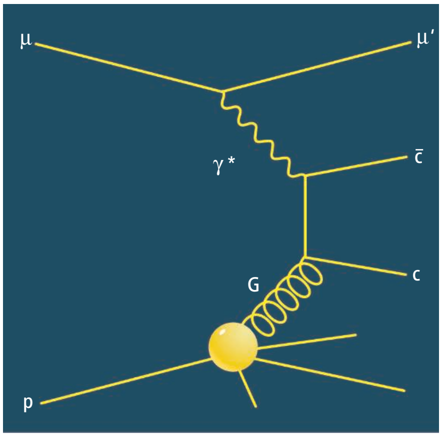
10.1126/science/1140737

PHYSICS

How Does the Proton Spin?

Steven D. Bass

Protons are made of quarks and gluons, but their spins don't add up. New experiments may help resolve this discrepancy.



Spin story. Physicists use Feynman diagrams such as this to express the sequence of events in a high-energy particle collision. In one type of experiment, a polarized muon (μ) and a polarized proton (p) approach each other on the left hand side. As they interact, the muon exchanges a polarized photon (γ). Pairs of charm-anticharm quark particles (c-$\bar{c}$)are produced; the precise number of these particles created depends on the spin of the gluons (G) in the polarized proton, which allows the spin of the gluons to be reconstructed.

Many particles, such as electrons, protons, and neutrons, behave like spinning tops. Unlike classical tops, however, the spin of these particles is an intrinsic quantum mechanical phenomenon. This spin is responsible for many fundamental properties of matter, including the proton's magnetic moment, the different phases of matter in low-temperature physics, the properties of neutron stars, and the stability of the known universe. In recent experiments, a number of research groups have been seeking to shed some light on the puzzling origin of spin and how this might resolve some large discrepancies between theory and experiment.

Particles such as the proton are actually combinations of more basic entities called quarks and gluons (which bind the quarks together). One of the challenges to physicists over the past 20 years has been to understand how the proton's spin is built up from its quark and gluon constituents. Models of the proton generally predict that about 60% of the proton's spin should be carried by the intrinsic spin of its three quarks, with the rest carried by orbital angular momentum (that is, the quarks flying around inside the proton). However, experiments at CERN (European Organization for Nuclear Research), DESY (Deutsches Elektronen-Synchrotron), and SLAC (Stanford Linear Accelerator Center) have taught us that the contribution from the spin of the quarks inside is small, only about 30% (*1*–*4*). This shortfall offers a substantial challenge to our understanding about the structure of the proton. To sort this out, a vigorous global program has produced about 1000 theoretical papers, and dedicated spin experiments are under way at CERN, DESY, Jefferson Laboratory, and RHIC (Relativistic Heavy Ion Collider) to map individual quark and gluon angular momentum contributions to the proton's spin. These experiments are now yielding exciting results (*5*).

The proton is described by quantum chromodynamics (QCD, the theory of quarks and gluons) as a bound state of three confined "valence" quarks (*6*). The quarks have spin 1/2 and interact through the exchange of gluons, which have a spin of 1 (where spin is quoted in units of Planck's constant divided by π). When we probe deep inside the proton, the strength of quark-gluon and gluon-gluon interactions is small because of "asymptotic freedom." This unusual idea means that, unlike some interactions, such as electrostatic forces, the force between quarks and gluons weakens as they get closer together. If a quark tries to escape, though, the force becomes stronger—so strong, in fact, that the quarks and gluons are always bound inside nuclear particles such as the proton; they are never observed by themselves as free particles.

In low-energy experiments, the proton behaves like a system of three massive "constituent" quarks carrying about 1/3 each of the mass of the proton. When we look deeper inside in high-energy experiments, these constituent quarks dissolve into near massless "current" quarks and a sea of quark-antiquark pairs and gluons.

The spin experiments at CERN, DESY,

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Jefferson Laboratory, and SLAC involve firing high-energy electrons or muons at a target of protons with aligned spins. The incoming electron interacts with a target proton by exchanging a high-energy photon that enables researchers to probe deep inside the proton. The photon can be absorbed by a quark polarized in the opposite direction to the photon but not by one polarized in the same direction as the photon. This allows us to extract information about the spin of the quarks when one controls the spin polarization of both the beam and the proton target. The RHIC spin experiments involve high-energy polarized proton-proton collisions, rather than electron-proton interactions.

In analyzing these collisions, the key questions (*7*) are: What happens to spin in the transition from current quarks (those probed in high-energy experiments) to constituent quarks (the building blocks of the proton)? How is the spin 1/2 value of the proton built up from the spins and orbital angular momentum of the quarks and gluons inside? Why is the measured quark spin contribution so small compared with quark model predictions? Is the "missing spin" a valence quark effect or attributable to the sea of quarks and antiquarks? Are the excitations of the quark-antiquark sea polarized in the opposite direction to the proton's spin (thus canceling some of the spin)?

The spin of the gluons that bind the proton can screen the spin of the quarks measured in high-energy experiments, making the spin look diminished. This effect is proportional to the gluon polarization Δg. But how large is this gluon polarization? The QCD vacuum is a quantum superposition of an infinite number of states characterized by nontrivial spin structure. When one puts a valence quark in this vacuum, its spin can become delocalized so that the total spin becomes a property of the proton rather than the sum over the individual quarks probed in high-energy experiments. How big is this effect?

Measurements by the COMPASS (Common Muon Proton Apparatus for Structure and Spectroscopy) Collaboration at CERN and the PHENIX (Pioneering High-Energy Nuclear Interaction Experiment) and STAR (Solenoid Tracker at RHIC) experiments at RHIC suggest that the gluon polarization is much too small to explain the difference between the quark model prediction of ~60% for the quark spin contribution and the measured value of ~30%, although it may still make an important contribution to the net spin of the proton (*5*, *8*). The COMPASS and RHIC experiments use different processes to access the gluon polarization. The COMPASS measurements are extracted from the production of charm particles (see the figure) and charged pions with large transverse-momentum in polarized muon-nucleon collisions. The RHIC measurements are extracted from high-energy particle production in polarized proton-proton collisions. Measurements of the sea polarization by the HERMES (HERA Measurement of Spin, where HERA is the Hadron Elektron Ring Anlage Accelerator at DESY) suggest that this is also small, too small to resolve the spin puzzle, and that the 30% quark spin contribution is approximately saturated by valence quark contributions (*9*).

New, more precise gluon-polarization measurements will soon be available from the 2006 data taken at COMPASS and RHIC. Independent measurements of the valence and sea-quark contributions will soon be available from COMPASS. It will be interesting to see whether these CERN data confirm the HERMES results. Experiments at Jefferson Laboratory are probing the spin properties of the valence quarks in kinematics, where they are sensitive to the confinement process. The planned 12-GeV upgrade of the facility will make vital contributions to our understanding of orbital angular momentum contributions to the proton's spin.

Spin measurements have a bright future and continue to challenge our understanding about the structure of the proton and fundamental aspects of quark dynamics. Much exciting progress has been made. The next years promise to be equally exciting.

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10.1126/science.1140165

IMMUNOLOGY

Asymmetry and Immune Memory

Dan R. Littman and Harinder Singh

Asymmetric cell division of lymphocytes ensures that our adaptive immune system maintains a balanced production of two different types of T cells.

Our adaptive immune system is endowed with an enormous repertoire of antigen-specific cells (B and T cells) that respond to and eliminate diverse pathogens. The system can also recall previous infections and respond more rapidly and effectively when reexposed to a pathogen, a feature known as immunological memory. How T cells differentiate into both short-lived effector cells that combat infections and long-lived memory cells that protect us for years has been a central question in immunology (*1*). On page 1687 in this issue, Chang *et al.* (*2*) propose that effector and memory T cells are simultaneously generated from the division (mitosis) of a T cell after it responds to a microbial challenge. T cells appear to have adopted an evolutionarily ancient means of asymmetrically partitioning cell fate determinants, thus ensuring balanced production of both T cell types and avoiding depletion of the T cell repertoire.

When microbial pathogens breach our mucosal barriers (such as the lining of the gastrointestinal or respiratory tract), the innate immune system responds by processing and presenting pathogen components to T cells. Microbial antigens are loaded onto major histocompatibility complex (MHC) molecules on the surface of dendritic cells, and thus interact with antigen receptors on the surface of pathogen-specific T cells. This interaction stimulates formation of an interface known as the immunological synapse (see the figure) and involves redistribution of other T cell surface components to the synapse, including coreceptor molecules CD4 or CD8, adhesion proteins (integrins), and cytokine receptors (*3*, *4*).

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