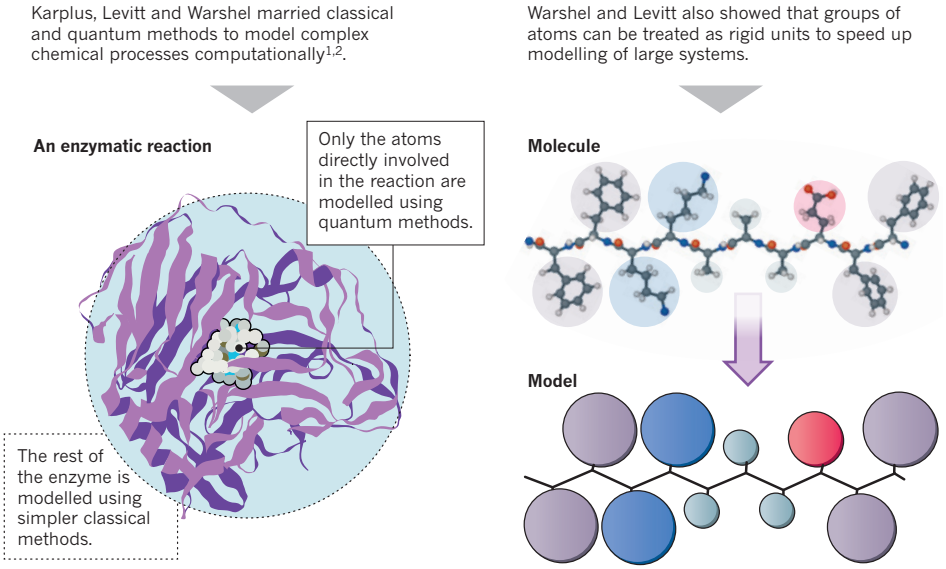
NOBEL 2013

As the recipients of the 2013 science Nobel prizes gather in Stockholm to celebrate and be celebrated, News & Views shares some expert opinions on the achievements honoured.

CHEMISTRY

Methods for computational chemistry

The Nobel Prize in Chemistry was awarded to Martin Karplus, Michael Levitt and Arieh Warshel for their work on developing multiscale models for complex chemical systems (see figure).



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MULTISCALE MODELS
by Walter Thiel

Complex chemical processes occur on different length- and timescales. Events that involve electrons, such as the making and breaking of chemical bonds, are localized in space and time. They need to be described by quantum mechanics (QM), whereas the influence of the environment and the slow motions of atoms during a reaction are normally well represented by classical molecular mechanics (MM).

The laureates were the first to propose a hybrid QM/MM approach for studying chemical properties and reactions, initially for the special case of planar molecules[1] and then as a general scheme for modelling enzymatic reactions[2]. This mathematical approach is essentially a marriage of Schrödinger's quantum theories and classical Newtonian ideas, combining the best of both worlds to enable tailor-made simulations of complex chemical processes.

The prizewinners' pioneering work in the 1970s provided explicit expressions for calculating the total QM/MM energy of a system and the QM/MM interaction terms. Advances by many research groups in QM and MM methods during the 1980s paved the way to breakthroughs for QM/MM modelling in chemistry in the 1990s. Major methodological issues were then solved by establishing suitable QM/MM interaction models and treatments for the QM/MM interface region, and efficient procedures were implemented for exploring large-scale QM/MM potential surfaces (which represent total energy as a function of atomic position). Since then, there has been an exponential growth in QM/MM applications[3], all underpinned by the original work of Karplus, Levitt and Warshel.

The concept of multiscale modelling is actually much broader than QM/MM, and so one can safely expect further progress towards an ever more realistic modelling of increasingly complex chemical processes.

COMPUTER EXPERIMENTS
by Gerhard Hummer

Multiscale molecular simulations, as pioneered by Karplus, Levitt and Warshel, proved to be versatile and powerful right from the start, revealing how receptors in the eye are activated by light, and how the resulting signals are passed on through changes in molecular conformation.

The laureates' approach allows each part of a molecular system to be described at the simplest level possible: as atoms, using quantum or classical mechanics; as classical pseudo-particles that represent multiple atoms; or, in the case of bulk solvent, as a continuous medium that lacks atomic detail[2,4]. Molecular interactions are captured by potential surfaces. Such potentials are now used routinely to determine protein structures from experimental data, to develop new drugs and to rationally design materials.

Simulations also provide fundamental insight into the function of biomolecular 'machinery' by revealing the underlying molecular motions and energetic driving forces. From photosynthesis to the processing of genetic material[5], enzyme-catalysed reactions have been modelled and followed atom by atom, bond by bond[3]. The dynamics of molecular motors that power muscle contraction or the synthesis of ATP molecules — a cell's source of energy — have also been simulated. Even the self-assembly of biomolecular machinery can be studied, from the folding of proteins[6] to the formation of entire organelles[7] and the protein shells of viruses[8].

With increasingly accurate representations of the energetics and dynamics of molecular systems, simulations yield detailed quantitative information and mechanistic insight that are unattainable in laboratory experiments. The vision of computational modelling as a

reliable substitute for actual experiments is thus becoming a reality. ■

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ECONOMICS

Predicting asset prices

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel was awarded to Eugene F. Fama, Lars Peter Hansen and Robert J. Shiller, whose empirical analysis of asset prices has shaped our understanding of how markets work (see figure).

EFFICIENCY AND VOLATILITY
by Christopher Polk

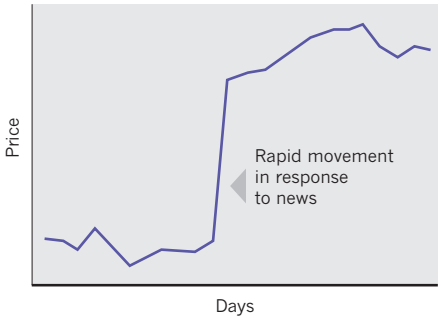
Fama's efficient market hypothesis (EMH) argues that competition among investors makes the return from using information on stock prices commensurate with the cost of that information. Thus, if costs are zero, prices correctly reflect all relevant information[1]. According to this hypothesis, if we could easily predict that stock prices will rise tomorrow, we would all buy today, such that prices would in fact rise today until they reflected the information we had received. Tests by Fama in the 1960s found that short-run returns were mainly unpredictable, which is consistent with a market that incorporates information efficiently.

Fama emphasized that the EMH was not directly testable; one can only test a joint hypothesis of the EMH and a model detailing the way in which expected returns are set. If, say, small-company stocks generally outperform large-company stocks, this might not indicate that the pricing of small companies is inefficient, but rather that small-company stocks are riskier and hence their investors demand high expected returns as compensation[2].

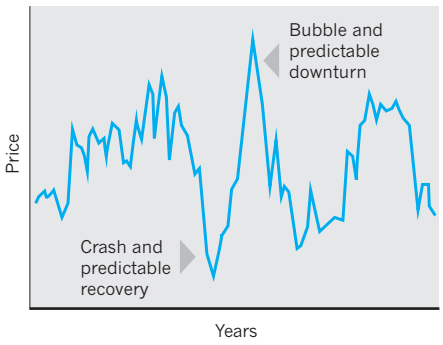
In 1981, Shiller showed that historical prices were excessively volatile relative to their future realized value[3]. This suggested that although prices respond quickly to information, they change for other reasons as well. Shiller interpreted this volatility as resulting from investor sentiment. Subsequent work linked excess volatility to predictable variation in long-run returns; short-term predictability was later found as well.

These findings presented a serious challenge to the EMH, but Fama's joint hypothesis allows a possible explanation: time-varying expected returns may be due to time-varying risk and/or risk aversion. Understanding the sources — rational and sentiment-based — of predictable variation in returns is at the heart of modern financial economics.

SHORT-TERM UNPREDICTABILITY
Fama showed that asset prices are extremely difficult to predict in the short term.



LONG-TERM PREDICTABILITY
But Shiller showed that there is greater predictability over the longer term, and interpreted this finding as market inefficiency resulting from investor behaviour.



TESTING THEORIES
Hansen's statistical techniques for testing economic theories highlighted the attractiveness of stocks to investors who can tolerate risk.

EMPIRICAL FINANCIAL ECONOMICS
by John Y. Campbell

Financial markets continually generate vast quantities of data on asset prices. Fama, Shiller and Hansen have led an effort, over almost 50 years, to use these data to better understand the economy and investor behaviour.

Fama observed that the return on any risky financial asset is the sum of a 'required' return that a rational investor expects to earn and an 'unexpected' return driven by the arrival of news. He noted that, over short time periods, the volatility of unexpected returns is much greater than any movement in the required return, and hence that short-term price movements accurately reflect the news hitting the market at each point of time.

Hansen built on Fama's insight, developing a powerful statistical method to extract from asset returns information about key properties of the economy, such as investors' average aversion to risk, without having to model other features of the economy that are irrelevant to the problem at hand[4,5].

Shiller pointed to data indicating that large price swings result from the accumulation of movements in required returns over long periods of time, and that unexpected returns reflect not only news about the future payments that assets will make, but also unexpected changes in the required return[6].

Together, their work has definitively shown the value of empirical research in understanding price formation in financial markets. Fama and Shiller have also used financial data to construct indexes that summarize the movements of broad categories of assets, such as groups of stocks with similar characteristics and houses in the same city[2]. ■

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