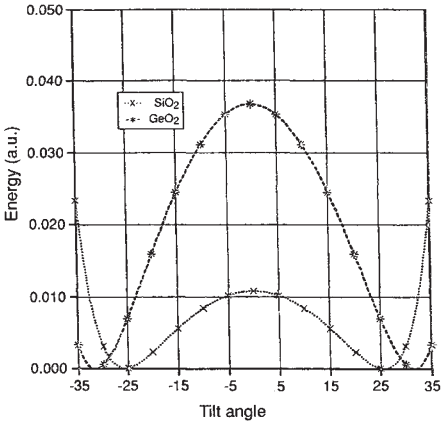

Unit-cell energy (a.u.) versus tilt angle for cristobalite SiO_2 (dotted line) and GeO_2 (dashed line). The origin of the potential corresponds to the α twinned structure.

from the α to the β structure by 0.018 a.u. in quartz and 0.014 a.u. in cristobalite. In fact, no net changes in ionicity between any of the crystal phases are predicted by our *ab initio* calculations on infinite crystals.

The Born–Oppenheimer energy curve $E(\delta)$ suggests that the high-temperature β phase can be viewed not as a minimum of the potential-energy surface but rather in terms of the expectation values of the atomic coordinates with respect to the nuclear wavefunction. Molecular dynamics calculations[4] provide support for this interpretation. Starting from the α_1 structure, the α_2 twin appears as the temperature is raised, and at 850 K the system alternates dynamically between the two phases. This corresponds to the appearance of a symmetric double-well potential in the Born–Oppenheimer energy surface (see figure). The soft-mode normal coordinate can be approximated by the tilt angle δ. For the symmetric double well, the expectation value $<\delta>=O$, corresponding to the β phase, whereas at low temperature the symmetry is broken and $<\delta>$ takes negative and positive values for α_1 and α_2, respectively. When the nuclei are considered as quantum particles, the α → β transition is displacive, in agreement with experiments[5], whereas a classical description corresponds to the dynamical picture of the molecular dynamics calculation[4].

As pointed out by Tsuneyuki *et al.*[4], the thermal energy required to symmetrize the potential increases with the height of the barrier separating the twinned structures. We calculate a higher barrier for GeO_2 than for SiO_2 (see figure), which explains why no β structure is observed for the germanium analogues of silica polymorphs.

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Calcium binding to fibrillin?

SIR — Dietz *et al.*[1] described an Arg 239→Pro mutation in one of the 34 epidermal growth factor (EGF)-like repeats of the filbrillin gene[2] found in two patients with Marfan syndrome. These repeats contain a consensus sequence (see diagram) analogous to that found in the first EGF-like domain of coagulation factor IX which is known to bind calcium[3]. It therefore seems likely that fibrillin will also bind calcium. Moreover, the two-dimensional NMR structure of the EGF-like domain[4] of factor IX suggests that Arg 239 in the analogous fibrillin EGF-like domain is located on the second strand of an antiparallel β-sheet adjacent to the inferred calcium binding site. We propose that local disruption of this calcium-binding site could be responsible for the defect in fibrillin function, although long-range effects of the proline substitution on protein structure cannot be excluded. Supporting the concept of local disruption is the identification of two mutations in the factor IX EGF-like domain, Asp 47→Glu and Asp 64→Asn, present in patients with haemophilia B. These mutations reduce calcium binding appreciably but do not grossly affect the protein's structure[3].

Several groups have proposed that EGF-like domains are involved in protein–protein interactions. We would like to draw attention to a recent paper[5] where *notch* and *delta*, two *Drosophila* proteins containing EGF-like repeats with the calcium-binding consensus, interact in a calcium-dependent manner. Could calcium interaction with EGF-like repeats in fibrillin be intimately linked with its function in connective tissue?

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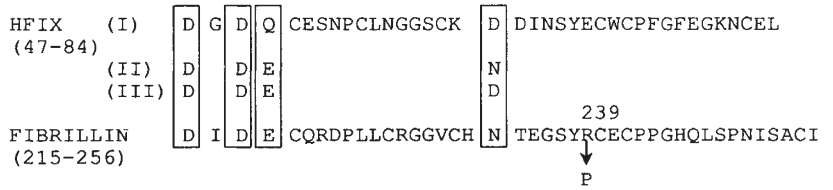

Amino acid residues important for calcium binding to the human factor IX (HFIX) EGF-like domain (I) are shown boxed with the analogous residues from one EGF-like domain of fibrillin. The position of the mutation Arg 239→Pro identified in two patients with Marfan syndrome is indicated. Variations of the calcium-binding consensus found in other proteins, which also bind calcium when introduced into factor IX are shown (II, III).

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Bell's inequality

SIR — Maddox's article[1] on non-locality in quantum mechanics reminded me that Bell's inequality has a long history which may be of some interest. A few years ago, I attempted to trace the origins of the probability metric. (The distance between two events is the probability that one of them occurs but not both. Strictly speaking, this is a pseudo-metric from which a metric can be constructed by standard techniques.) My colleague, D. A. Edwards, pointed out that the treatise by Dunford and Schwartz[2] contains both a discussion of a more general metric on measure spaces and a survey of its history. There it is traced back to work of Aronszajn and Nikodým[3] in the late 1920s. Moreover, that metric is actually just a special case of the L^1 metric on integrable functions discussed 10 years earlier by Fréchet[4]. (One restricts the L^1 metric to indicator functions of events.)

The fact that the basic inequality was known for so long makes it all the more surprising that, until Bell's independent rediscovery of it in the 1960s, no one seems to have observed that the triangle inequality fails in quantum mechanics and can therefore provide a test of large classes of hidden variable theories. The new paper by Fivel[5], which Maddox discusses, provides an interesting new insight by comparing the probability metric with the quantum-mechanical Hilbert space metric and thereby isolating the mechanism which gives rise to Bell's inequality in one case but not in the other.

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