catalysed *cis*-to-*trans* isomerization of *N*-succinyl-Ala-Ala-*cis*-Pro-Phe-pNA (ref. 2). This observation strongly suggests that the imidazole of an active site His is not involved in catalysis. Third, there is no solvent deuterium isotope effect on k_c/K_m for the cyclophilin-catalysed *cis*-to-*trans* isomerization of *N*-succinyl-Ala-Ala-*cis*-Pro-Phe-pNA (ref. 2). This eliminates mechanisms involving general-acid/general-base catalysis such as that advanced by Kallen *et al.* in which His 126 is proposed to act as a general-base catalysis in isomerization.

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KALLEN *ET AL.* REPLY — In our paper on the structure of cyclophilin, a preliminary fit of the tetrapeptide substrate into the 2.8-Å electron-density map was modelled with the peptide in an all-*trans* conformation, with Arg 55 directly hydrogen-bonded to, and His 126 some 5 Å away from, the prolyl amide bond. This geometry suggested a mechanism in which a putative water molecule hydrogen-bonded to the histidine could mediate the *cis–trans* isomerase mechanism.

The experimental results summarized by Stein suggest that water and His 126 are not involved in the mechanism for *cis–trans* isomerization. Recent refinement of the crystal structure using additionally collected high-resolution data (R=17.8% for all data to 2.3 Å) shows a good fit for the alanyl–prolyl amide of the tetrapeptide in the *cis*-conformation, with His 126 in close contact to the alanyl–prolyl carbonyl oxygen.

This higher-resolution X-ray refinement of the cyclophilin–tetrapeptide structure thus indeed does not confirm the presence of a bridging water molecule in the active site, but does show that His 126 (and Arg 55) are involved in substrate binding. Our conclusion that Arg 55 and His 126 are important residues in the *cis–trans* isomerase mechanism has also been further substantiated by site-directed mutagenesis experiments (M. Luyten *et al.*, in preparation). A publication presenting the fully refined structure and the detailed interaction of the tetrapeptide with cyclophilin is in preparation.

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1. Kallen, J. *et al. Nature* **353**, 276 (1991).
2. Harrison, R. K. & Stein, R. L. *Biochemistry* **29**, 1684–1689 (1990).
3. Harrison, R. K. *et al. J. Am. chem. Soc.* **112**, 7063–7064 (1990).
4. Stein, R. L. *Curr. Biol.* **1**, 234–236 (1991).

Short-range flaws

SIR — Maddox[1] reports the claim by Suzuki[2] to have dealt with short-range divergence problems in quantum electrodynamics (QED) in such a way that the subtraction of infinite quantities from each other would be avoided. This result would render the so-called renormalization procedure obsolete; unfortunately a study of the derivation reveals some basic flaws in the argument.

Suzuki[2] introduces a unitary transformation which splits the hamiltonian H for the electron–photon system into two parts: H_1 and H_2. Because both derive from the same photon field, these two operators do not commute. However, Suzuki explains his neglect of the corresponding commutator by (wrongly) invoking relativistic invariance. Such illicit manipulation is further demonstrated when the following surprising formula is proposed for the scattering S-matrix:

$$\exp\left[-i\frac{1}{2}\int_{-\infty}^{+\infty}(H_1+H_2)\,\mathrm{d}t\right] \rightarrow \frac{1}{2}\left[\exp\left(-i\int_{-\infty}^{+\infty}H_1\mathrm{d}t\right)+\exp\left(-i\int_{-\infty}^{+\infty}H_2\mathrm{d}t\right)\right]$$

Even if the commutator were to vanish, one would get the S-matrix in factorized form and not as a sum. Anyway, one cannot neglect the commutator of H_1 and H_2 which allows quantum-exchange processes that are missing in Suzuki's work, giving rise to charge and mass renormalization.

What are 'renormalizable' theories? It may be that a finite theory could be derived to unify all the known forces. Such a possibility is offered by the so-called string theories that have undergone intense study[3]. In a truly finite theory with only one parameter with a physical dimension, it should be possible, in principle, to compute the mass of the electron or the coupling constant of QED, $\alpha = e^2/\hbar c \sim \frac{1}{137}$. In contrast, in a renormalizable theory such as QED, there are divergences that are absorbed in parameters such as electron mass and coupling constant α, adjusted to their experimental values. In this scheme, QED would be an effective theory for the low-energy limit of a more fundamental theory.

In condensed-matter physics, the application of field theory to the study of critical phenomena has also emphasized the nature of a renormalizable theory[4]. It emerges as the long-wavelength limit of a microscopic theory containing a small physical length scale that suppresses the short-range divergences. In a solid-state system, the lattice spacing sets an upper bound to the allowed momenta in otherwise divergent (Feynman) integrals. In polymer physics the size of the chemical bonds provides this scale, much smaller than the size of the macromolecule[5].

Another striking example can be found in quantum chromodynamics (QCD). This gauge field theory, which is renormalizable, provides a description of strong interactions, the experimental successes of which have been reported[6]. On the theoretical side, this field theory has been recently derived[7] as the low-energy limit of a particular finite string theory. The infinities of the limiting renormalizable field theory, that is, QCD, appear in the formal mathematical limit where the length scale built into the string theory tends to zero. In unified theories based on strings[3], this length scale is expected to be the Planck length constructed from Newton's constant G, $\hbar$ and c, and which is of the order of 10^{-33} cm.

Returning to QED, it should be the effective description of electromagnetic processes at distances much larger than the Planck length. Presently, its closed form is relativistically covariant, and, after renormalization, leads to finite answers to all orders in perturbation theory. The perturbative calculation of the gyromagnetic ratio of the electron (the Landé factor), in excellent agreement with experiments, certainly include mass and charge renormalizations. Such effects are absent in Suzuki's paper as his neglect of the cross-processes leads to no mass renormalization at all. It is implausible that a simple trick could fundamentally alter the present status of QED, the most accurate physical theory ever built.

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1. Maddox, J. *Nature* **353**, 497 (1991).
2. Suzuki, R. *Il Nuovo Cimento* **104**A, 1115–1125 (1991).
3. Green, M., Schwarz, J. H. & Witten, E. *Superstring Theory* (Cambridge University Press, 1987).
4. Wilson, K. G. *Rev. Mod. Phys.* **47**, 773–840 (1975).
5. de Gennes, P. G. *Scaling Concepts in Polymer Physics* (Cornell University Press, Ithaca, 1979).
6. Close, F. *Nature* **353**, 498–499 (1991).
7. Bern, Z. & Kosower, D. A. *Phys. Rev. Lett.* **66**, 1669–1672 (1991).

Scientific Correspondence

Scientific Correspondence is intended to provide a forum in which readers may raise points of a scientific character. They need not arise out of anything published in *Nature*. In any case, priority will be given to letters of fewer than 500 words and five references.