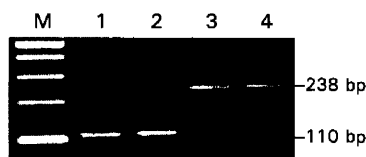
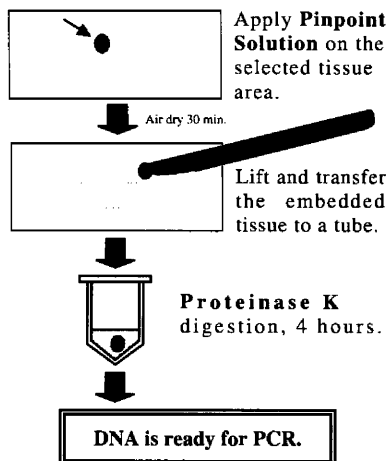


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yond the sequence itself, the process by which it is obtained is important. The extent to which it is possible to operate in a "best behavior" mode will be instructive in assessing DNA sequencing performance. At the very least, such trials will establish a lower limit to the error rate expected. Given that gold standards would imply only a minor increment to the resequencing load, it would seem prudent to include them, even if, as some claim, "one already knows the answer."

2) Green's use of the imprecise phrase "tend to" in his third paragraph illustrates the quality standard point we wished to make. A quantitative study of how scientific utility and cost vary with sequence accuracy would seem essential to setting the specifications for the project and does not seem an impossible task.

3) Computer simulation has proven to be an extraordinarily useful tool to understand and optimize all manner of complex natural and artificial systems; the sequencing process should be no different. Useful simulations require that one understands the distribution and correlation of errors. Acquiring such understanding requires careful and targeted process experiments, which are quite distinct from production sequencing. The report advocates that the time and resources be expended to do these experiments, so that high-fidelity simulations can be constructed and exploited.

As Green notes, fusing the languages and approaches of different disciplines toward a common challenge is often a separate challenge of its own. This latter can be met only by a continuing dialog in which all parties are both students and teachers.

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α -Synuclein Gene and Parkinson's Disease

Mihael H. Polymeropoulos *et al.* (Reports, 27 June 1997, p. 2045) (1) reported an Ala53Thr mutation in the α -synuclein gene, at the PD-1 locus on chromosome 4q21-q23 (2), in a large Italian family and three smaller Greek kindreds with autosomal dominant Parkinson's disease (PD). The phenotype in the Italian family, however, differs slightly from idiopathic Parkinson's disease, with earlier onset and a more rapid disease progression (3), and linkage to this locus has been excluded in most of the tested families (Technical Comments, 18 July, pp. 387 and 388; Letters, 14 Nov., p. 1212; corrections,

5 Dec., p. 1696) (4). These studies (4), however, provide only indirect evidence that the PD-1 locus might rarely be involved in familial Parkinson's disease. The frequency of α -synuclein gene mutations in dominant Parkinson's disease remains to be determined.

We have examined the entire coding sequence of the α -synuclein gene in 25 families with dominant Parkinsonism. Families were selected with the use of the following criteria: (i) presence of at least two affected first-degree relatives in two successive generations; (ii) definite Parkinson's disease characterized by two of four essential signs (bradykinesia, rigidity, resting tremor, or asymmetrical onset); (iii) marked improvement of symptoms after administration of levodopa, except for two de novo cases; and (iv) absence of the exclusion criteria (supranuclear ophthalmoplegia, cerebellar or pyramidal signs, apraxia, severe autonomic or postural disturbance, or dementia within 2 years of onset).

Twenty-four of these families were French, and one was Italian. There were 13 men and 12 women among the index cases. The mean age at onset of the index cases was 54 ± 16 years (range, 28 to 77 years). We did not observe severe dementia in any patient. After DNA extraction from lymphoblasts, the entire coding region of the longest form of the α -synuclein gene, which encodes a protein of 140 amino acids, was amplified by reverse transcriptase polymerase chain reaction and directly sequenced as previously described (5). We did not find any mutations or polymorphisms in the index cases of any family. Vaughn *et al.* (6) have reported not finding the Ala53Thr mutation in 230 cases of familial Parkinson's disease, but they searched only for this specific mutation. We have confirmed that the Ala53Thr mutation is rare in Parkinson's disease. We also found—in a large series of families with dominant Parkinson's disease—no other mutations anywhere in the coding sequence of the α -synuclein gene. Therefore, unless mutations are present in other, noncoding regions of the α -synuclein gene (that is, in promoter or regulatory sequences), PD-1 could only represent, at best, a minor locus for dominant Parkinson's disease in our study population.

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7. The French Parkinson's Disease Genetics Study Group: Johann Tassin, Alexandra Dürr, Nacer Abbas, Anne-Marie Bonnet, Marie Vidailhet, Soraya Medjbeur, Christiane Penet, Yves Agid, and Alexis Brice, INSERM U289 and Fédération de Neurologie, Hôpital de la Salpêtrière, 75651 Paris Cedex 13, France; Michel Borg, Hôpital Pasteur, 06006 Nice Cedex, France; Emmanuel Broussolle, Hôpital Neurologique, 69003 Lyon, France; Alain Destée, Centre Hospitalier Régional (CHR), 59034 Lille Cedex, France; Frank Durif, Hôpital Fontmaure, Chamalières, France; Josué Feingold, INSERM U155, 75005 Paris; Gilles Fénelon, Hôpital Tenon, Paris; Jean-René Fève, Hôpital Laënnec, 4035 Nantes Cedex, France; Maria Martinez, INSERM U358, 75475 Paris; Pierre Pollak, Centre Hospitalier Universitaire (CHU), 38043 Grenoble Cedex 9, Switzerland; Olivier Rascol, Hôpital Purpan, 31073 Toulouse Cedex, France; François Tison, Hôpital Pellegrin-Tripode, 33076 Bordeaux Cedex, France; Christine Tranchant and Jean-Marie Warter, CHR, 67000 Strasbourg, France; Marc Vérin, Hôpital de Pontchaillou, 35033 Rennes Cedex, France; Francois Viallet, CHU, 13616 Aix-en-Provence Cedex, France.
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discussions and the Association France Parkinson, the Assistance Publique-Hôpitaux de Paris, and the European Community Biomed 2 (BMH4CT960664) for financial support.

Universal Quantum Simulators: Correction

Several readers have pointed out an error in my Research Article "Universal quantum simulators" (23 Aug. 1996, p. 1073) (1). On page 1076, after equation (2), I incorrectly cited K. Kraus as showing that it is always possible to mimic the effect of an environment for an N -qubit quantum system by using a simulated environment consisting of N qubits (2, which is reference 39 in the article). In fact, the implication of Kraus's work (2) is that it is always possible to simulate such an environment using a simulated environment with $2N$ qubits, not N . An N -qubit simulated environment clearly suffices in some cases: that it always suffices should be considered to be a conjecture that the set of equations given by equation (2) always possesses a solution. However, the minimum size of a simulated environment sufficient to model any environmental interaction is not currently known. The conclusion of my article, that a quantum com-

puter can efficiently simulate any quantum system that evolves according to local interactions, remains unchanged.

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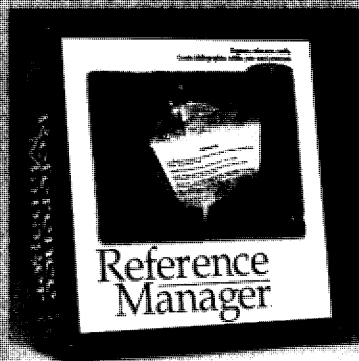
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