DISTRIBUTION OF POINT MUTATIONS

Mutational type	Germline cells: Factor IX Caucasians*	Factor IX Asians	Neoplastic cells: p53 Colon	p53 Bn/Br	Rb Retina	p53/Rb Lung
Transitions	31	10	11	6	5	0
(Transitions at CpG)	(12)	(6)	(6)	(3)	(3)	(0)
Transversions	5	4	2	0	1	8
Micro-deletions/insertions	2	2	2	0	2	1
Ref.	2	3	4,5	5	6	5–8

*The data approximate the underlying pattern of germline mutation in factor IX. Transitions at CpG are elevated 24-fold relative to other transitions (ref. 2). When the subset of Caucasians with severe disease was compared with the Asian sample, the patterns were essentially identical. The excess of deletions in retina cells reflects the large and highly redundant nature of the retinoblastoma (Rb) protein. Five of the six base substitutions produce nonsense or splice junction defects, implying that the more numerous missense mutations are underrepresented because they generally do not cause disease.

pattern of germline or somatic mutation will commonly be the same. It seems most likely that there is a strong selective pressure for endogenous control of the mutational process, rather than a ubiquitous and prominant mutagen. For germline mutation, the rate may be constrained by opposing evolutionary forces. Too little germline mutation would result in extinction of the species, as the level of variation in the population would be insufficient to adapt to environmental changes. Conversely, more than the requisite amount would increase the morbidity of the species as virtually all disease has a genetic predisposition.

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Sensing reducing gases

Sir—The recent report[1] of a novel thin-film electrochemical cell for energy conversion prompts us to describe some work we have been carrying out using a related concept for the purpose of detecting reducing gases such as hydrogen and carbon monoxide in air.

Our cell is shown schematically in Fig. 1. Its solid components are a porous oxide substrate (polymer substrates, as described in ref. 1 are also useful) and two electrodes of dissimilar metals which are deposited by d.c. sputtering. For an electrolyte we depend entirely on a film of moisture adventitously absorbed from the atmosphere onto the surface of the substrate between the electrodes. With electrodes of platinum and gold, respectively, and the cell exposed to air in the relative humidity range between around 20 and 100% at room temperature a substantial open circuit potential (up to 500 mV) is generated. Operation requires the presence of both oxygen and water vapour.

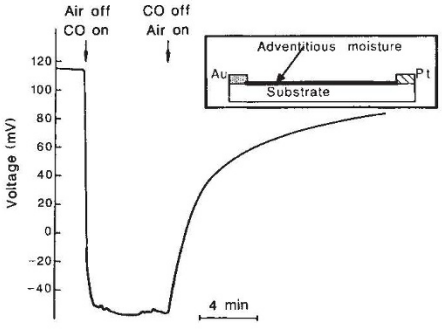

FIG. 1 Voltage response of WO_3 to 1% CO in air. Open-circuit potential from a cell based on a porous pellet of tungsten trioxide with platinum sputtered on to one flat surface and gold on the other. The potential difference was monitored via a Keithley model 614C electrometer with the platinum electrode connected as positive. The atmospheric compositional change between air and air containing 1% carbon monoxide at the points marked gave rise to a change of over 150 mV in the open circuit potential of the cell. Inset: schematic of the thin-film electrolytic cell.

The geometry of the three-phase interface involving a film of adsorbed moisture is ideally suited for sensing gas reactions: changes in open circuit potential result when the cells are exposed to small concentrations in air of a range of gases including hydrogen, carbon monoxide, ammonia, hydrogen sulphide and ethanol vapour (Fig. 1). The open circuit potential change of the cell increases approximately as the log of the concentration of the reducing gas in an air ambient (Fig. 2).

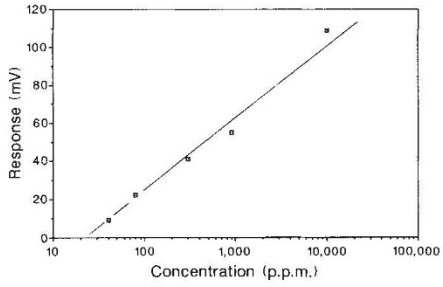

FIG. 2 Variation in the magnitude of the change in potential of a cell based on a porous pellet of tin dioxide, with one electrode platinum and the other gold as a function of the logarithm of the concentration of hydrogen in air.

We believe the mechanisms of response as involving changes in "mixed potentials"[2], which are different on different metals. An electrode at open circuit adopts a potential (mixed potential) such that the rate of all the anodic and cathodic processes balance. In air, in the absence of any other gases, the processes are the reduction of oxygen, and the reduction and oxidation of the metal:

$$\tfrac{1}{2}O_2 + H_2O + 2e^- \rightleftarrows 2OH^- \quad (1)$$

$$Pt + 2OH^- \rightleftarrows PtO + H_2O + 2e^- \quad (2)$$

$$Au + 2OH^- \rightleftarrows AuO + H_2O + 2e^- \quad (3)$$

The balance between reactions (1) and (2) establishes a different potential from that between reactions (1) and (3), hence accounting for the open-circuit potential difference of the cell. The presence of a fuel gas such as CO introduced the possibility of a different reaction:

$$CO + 2OH^- \rightleftarrows CO_2 + H_2O + 2e^- \quad (4)$$

which we surmise affects the mixed potential predominantly on the platinum electrode rather than on the gold, and hence gives rise to a change in the output of the cell.

As in the case of the thin-film electrolyte fuel cell[1], our device exhibits the convenient attributes of operating at room temperature and functioning without the need to separate the analyte (fuel) gas from the oxidant. The key role of reaction kinetics is also common to both applications.

For sensor applications the cell we have described offers a number of useful features: independence from the need for a reference volume leads to simplicity; room-temperature operation renders the detection of potentially flammable gases such as hydrogen a safer prospect and the open circuit potential in air provides a useful 'condition safe' indicator.

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2. Charlot, G., Badox-Lambling, J. & Trémillon, B. *Electrochemical Reactions: The Electrochemical Methods of Analysis* 271–307 (Elsevier, Amsterdam, 1962).

Scientific Correspondence

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