

Naturally, there is a real-space structure corresponding to the FCI geometry in 6D space whose reciprocal space is a BCI lattice. Clearly, there is an overall change in the diffraction patterns without disturbing the intense peaks. This indicates some sort of ordering reaction on the parent structure. Thus it has been proposed that partial ordering or short-range ordering leads to the arcs of diffuse intensity and perfect or long-range ordering gives rise to the superlattice spots, which changes the space group of the lattice in 6D space. From the quasicrystalline framework it is obvious that there is a realistic possibility of a disorder-order transformation in the icosahedral phase. However, the ordering in atomic scale is not yet known; first one must know where the atoms are in the quasicrystalline model. Work is in progress to resolve the issue with the help of 6D crystallography. Nevertheless, from geometrical considerations, the ordered structure in real space can

be realized as an FCI-type superstructure of the SI lattice. One has to wait and see whether or not a BCI-type superstructure of SI is possible in any other alloy system. It is pertinent to point out that the diffraction patterns from Al-Fe-Cu and related alloy systems show evidence of FCI ordering of the SI structure in real space even without annealing<sup>11, 12</sup>. The long-range-ordered quasicrystals are highly stable and can be grown to a larger size suitable for single-crystal X-ray studies. These experiments are expected to yield more interesting data which will help to understand the structure of quasicrystals in the near future.

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## Electronic device screens chemicals for biological activity

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A new device invented at Stanford University, called a silicon microphysiometer, now allows routine measurement of the metabolic responses of cells to physical and chemical stimuli<sup>1</sup>. The principle that this device taps is that all biological, chemical or physical changes in the environment of a cell are reflected in changes in the concentration and flow of molecules within the cell. The extensive interconnection among the different biochemical processes allows the detection of a response that is only indirectly associated with the primary stimulus.

Catabolic processes are ideal candidates for the indirect detection of responses. The primary catabolic products in mammalian cells, carbon dioxide and lactic acid, cause changes in acidity in the environment of the cells, which therefore reflects the metabolic

activity of the cells. The silicon microphysiometer, developed by Molecular Devices Corp., Menlo Park, California, uses light-addressable potentiometer sensors (LAPS) to measure changes in pH in the culture medium surrounding a small number of cells. It consists of a microvolume flow chamber in which the cells to be tested are immobilized. One wall of the chamber is the silicon-based LAPS. Apposed to the sensor, 100  $\mu$ m away, is a coverslip with the adherent cells. Medium is pumped through the channel between the sensor and the coverslip. The medium, differing from normal growth medium in lacking bicarbonate, has reduced buffer capacity and thus enhances pH changes. For measurement of metabolic rate, flow of medium is halted for 30 to 200 seconds. Cells acidify the medium in the chamber because of production of lactate and

some carbon dioxide. When flow is resumed the pH in the chamber rises and then returns to the pH of fresh medium. The rate of acidification of medium, measured by the microphysiometer, is a measure of the metabolic rate of the cells.

The immense potential of the device has been demonstrated in a recent study that evaluated the use of this instrument for continuous monitoring of receptor-mediated changes in the metabolic rates of living cells<sup>2</sup>, demonstrating the instrument's utility in screening new therapeutic drugs by measuring cellular responses accompanying receptor-ligand interactions. The expected qualitative effects of various nonspecific toxic chemicals on the metabolic rates of cultured cells have also been seen in experiments that employed the microphysiometer.

## RESEARCH NEWS

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The responses of the same receptors in different cell types and different receptors in the same cell type were studied. The  $\beta_2$ -adrenergic and  $m_1$  muscarinic acetylcholine receptors, each representative of a major neuroreceptor class in the sympathetic and parasympathetic nervous systems, were investigated. Both are known to function through guanine nucleotide-binding proteins (G proteins). The responses were demonstrated in three different cell types, viz. human keratinocytes, Chinese hamster ovary (CHO) cells and murine fibroblasts, with receptors that use three different second-messenger systems.

These studies, which used the microphysiometer, showed that an increase in cellular metabolic rate is a general response of a cell to hormonal stimulation, and that responses are receptor-specific. Cells that express transfected receptor genes respond only to the appropriate hormone or transmitter. These studies also document specificity of responses using pharmacological antagonists<sup>2</sup>.

Thus, among its many capabilities, the device can be used to:

(i) measure the metabolic response of tumour cells to chemotherapeutic agents,

and thus be used to screen compounds for potential anticancer activity;

(ii) measure the responses of human cells to chemical irritants by *in vitro* toxicological assays, which can serve as a replacement for the controversial rabbit-eye Draize test of ocular irritancy; (iii) trace the effect of virus infection on cells as well as the efficiency of antiviral agents at inhibiting the infection; and (iv) measure direct responses of cells following ligand binding to receptor.

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