

strated the chemical union between these normally incompatible groups, by synthesizing an intermetallic compound of K and Ni at pressures of the order of 310,000 atmospheres (31 GPa) and above at temperature of 2500 K developed in a laser heated diamond anvil. This unconventional union of K and Ni prompted them to speculate that 'since charge densities of Fe and Ni are similar, despite lower electronegativity and work function of Fe', K and Fe should also react under core pressure and suggested possibility of K as a probable component to lighten the core density^{6,7}. The other view that Si or S may be the light element in the core^{8,9} has problems with respect to oxidation states. Sulphur alone cannot satisfy the observed deficiency in core density without incorporation of another lighter element. Thus Si and S are suggested as the density-lightening elements and that early core formation is thought to have taken place under reducing conditions, facilitating dissolution of Si in the metallic core. Progressively, the conditions became oxidizing with addition of S to oxidize Fe to silicate⁵.

Now in a very recent work, Takuo Okuchi (Department of Earth and Planetary Sciences, Tokyo University, Japan) has resurrected the disfavoured H and experimentally demonstrated how indeed it can be the dominant element lightening the density of molten iron in the outer core¹⁰, though not as solid H as was once thought. He feels that contrary to the notion that considerable H escaped during the early degassing phase, it was actually incorporated into the segregating iron core quite early in primordial earth. Okuchi envisages sequence of reaction thus: assuming an initial H₂O content of 2% in primordial molten earth, he proposed segregation of H and ferrous Fe

from the primitive bulk through interaction of H₂O and metallic Fe. The H thus released, which estimates show is much more than what is contained in the hydrosphere, would have to dissolve into the core rather than diffuse and escape out of the earth. He has demonstrated these reactions experimentally under ultra high pressures generated in an uniaxial multi-anvil apparatus. The experiment is based on the fact that Fe and H react to form metallic hydride—FeH_x, a compound stable at pressures >5 GPa, but decomposing at pressures lower than this. In order to determine the partitioning coefficient of this metal-silicate bond and extrapolate the parameters to core conditions and evaluate the reactions, he reacted mixtures simulating an ultrabasic bulk-composition of iron and silicate components. He used a mixture of metallic Fe, MgO, brucite ([Mg(OH)₂], silica glass (SiO₂), silicic acid (SiO₂·0.4H₂O) and liquid H₂O under 7.5 GPa pressure and synthesized a solid compound FeH_{0.33}. This compound [m.p. between 1100 and 1200°C, about 600°C below that of Fe (melting point of Fe is reduced by addition of H)], melts to a liquid with a composition FeH_{0.4} in molten silicate; but being immiscible in a silicate melt, it rapidly breaks down as large droplets, and being unstable at available ambient pressure, quickly decomposes further into H₂ and Fe. In this confined state, hydrogen released is incapable of diffusing out and hence remains in the core.

Okuchi feels that (i) metal-silicate melt partitioning of H in primordial earth had occurred at the 'bottom of magma ocean where molten metal may have stagnated as iron ponds'; (ii) Most of H₂O accreted to earth should have dissolved into the magma ocean; (iii) If the pressure at the bottom of the magma ocean was

≥ 7.5 GPa, more than 95% of H₂O accreted to earth should have reacted with Fe to form FeH_x; (iv) Iron pond then sank to the core by large scale gravitational instability during which pressure and temperature adjacent to molten iron increased; (v) H partitioned into the molten iron at the bottom of magma ocean cannot return to silicate melt and should have gone to the core; (vi) This H would then reduce the density of iron in outer core by 5.5% and together with contribution from S (1.1%) and C (2.2–2.7%), the overall density reduction in outer core is ~9.9% which agrees with observed deficit. In the inner core also H may be the primary light element to explain the density deficit of about ~7.1%. However, Wood (Department of Geology, University of Bristol) observes that Okuchi's single stage model should be tested at realistic core pressures and actual core properties, in addition to testing the agreement of siderophile element depletion patterns accompanying FeH_x segregation².

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OPINION

Patents on life forms: the case for

J. Gowrishankar

The interrelated issues of intellectual property rights (IPRs), patents, biopiracy and India's stand *vis-à-vis* the World Trade Organization (WTO) have genera-

ted considerable debate and controversy amongst the lay public, non-governmental organizations, the executive arm of government and parliamentarians alike.

India's decision in 1994 to be a signatory to the set of final agreements emanating from the Uruguay Round of Multilateral Trade Negotiations (including

that to become a member of WTO) was based largely on the following premise: that the country stood to gain far more from the expected liberalization of international trade in the agriculture, textiles and services sectors than what it might lose from the fact that it was now also committed to amend its laws on IPR so as to provide adequate protection to inventions relating to new categories of medicines and to new plant varieties. Furthermore, it was also clear that should India choose not to be a signatory, it may perforce have to end up negotiating far tougher bilateral agreements with each of its trading partners.

One issue that has arisen, as a consequence of India joining the WTO, is the need for providing IPR for 'microorganisms' and for 'microbiological' processes in the country's patent system. That is, we have now to decide how, and to what extent, should protection in the form of new patent laws be provided for the commercial exploitation of life forms. A. V. Ganesan (former Union Commerce Secretary and the chief negotiator for India in the Uruguay Round) has indicated that the 'patenting of biological material raises a whole range of . . . ethical, moral, social and religious issues . . . [which] have not been resolved satisfactorily even in the industrialized world'. Others such as Suman Sahai (of the organization Gene Campaign) have argued that economic considerations must take precedence over the scientific in deciding a patent policy for microorganisms.

It is important to clarify one popular misconception before discussing this issue further. Microorganisms, or for that matter any life forms, are not patentable *in their natural state or habitat*. If an individual were to find an hitherto unidentified organism in the wild, such a finding comes under the category of a discovery and not an invention, and hence is not patentable. One important criterion for the issue of a patent is novelty, that is, the item or process in question must not have existed (not merely that its existence was not known) earlier.

My own suggestion on the question of the patenting of microorganisms differs significantly from those voiced earlier. I would maintain that India's position be no different for microorganisms than it is for IPR on other categories of material inventions. In other words, if we accept (or are compelled to accept) the notion

that (i) the invention of a material product or of a process to manufacture such a product, or (ii) the discovery of a new use for a known product, is an intellectual property owned by the inventor whose right is entitled to protection under the laws of the land, then the mediation of microorganisms in implementing the invention must not by itself negate any of the rights of the inventor.

The rationale for this opinion is that there is no conceivable difference between the inventive step(s) that employ a microorganism from those that do not. Hence any exception that is made in the case of the former will, in common sense, be arbitrary and discriminatory. Analogously, one could arbitrarily stipulate, for example, that any invention which employs a spring-mounted screw as one of its components (or, as another more extreme example, any chemical molecule that has three times as many H atoms as it has O atoms) is not entitled for protection under IPR. On what basis can microorganisms, or processes that employ them, be generically excluded from consideration as inventions under an IPR regime?

The argument that microorganisms are living entities and therefore that they can be considered as special entities for the purpose of IPR is a weak one. If people can own and breed race horses, or can grow cattle, poultry or crop plants for profit, there is no justification for the exclusion of microorganisms, and the ownership thereof, from similar commercial exploitation. It would be specious to argue that patenting of microorganisms should be denied on the grounds that such patenting would offend 'public order' or morality.

Arguably, the special exemption against the application of the IPR laws to any category of living beings can apply only to humankind – because of current social acceptance of the fundamental civil rights of every individual. Please note that this exemption also stems because of the evolution of human thought *vis-à-vis* the dignity of fellow individuals in the last 150 years, and this exemption is therefore just a sign of the times in which we live. In the early 19th century, when human slavery and slave trading were accepted social norms, one could have argued that IPR be extended to humans as well! I understand that I risk being pilloried if quoted out of context, and I

agree too that mine is an extreme position, but it appears to be the only rational one. Who knows, as humans become more 'emancipated', they may confer civil rights to other living species as well in which event there would be a case for exempting the latter too from IPR.

In my opinion, therefore, the law must permit individuals to enjoy IPR protection of any non-human living entity, provided that the other standard conditions for purposes of definition of an invention are satisfied. Thus for claiming protection, there must be a demonstrable 'inventive' step(s) involved which was neither available nor obvious to a skilled person in that field – such as clonal purification of a useful organism from the wild, creation of a defined mixture of organisms for a definite purpose, establishment of cell lines from an organism, genetic modification of an organism in the laboratory, or discovery of a new use for an organism. Obviously, genes or proteins that are obtained from living organisms would also be patentable as novel 'compositions of matter' (that is, as non-living chemical products) in their own right. It may be noted that this position is even more 'liberal' than that required of us by the WTO, which permits the exclusion of life forms such as 'plants and animals' from patentability.

Another question often raised is that an organism is the product of millions of years of evolution in nature, and how can one then justify conferment of IPR to an 'inventor' who makes just one additional modification to it? My answer is in three parts: (i) Such a question is not unique to IPR considerations only of living entities; the vast majority of material (i.e. non-living) inventions also represent incremental modifications of previously known complex entities. (ii) The IPR protection is given only to the modified organism, and the public is free to use the unmodified organism without infringing IPR. (iii) Finally, the conferred IPR is but a limited-term monopoly, and 15 or 20 years is a negligible time period in the context of human history. After this period, the modified organism of course becomes part of the public domain.

On the related question of IPR for new plant varieties, M. S. Swaminathan and others have argued that a proportion of the commercial value of a particular variety must go back to the traditional farming communities that had nurtured

these plants and gradually improved upon them over several millennia. That is a wonderful concept, but is unworkable for all generic inventions if taken to its logical conclusion – because logically then, every intermediary in the improvement process must also be entitled to a share of the IPR. I illustrate its unworkability with an example from medicine.

It was known several centuries ago to the Anglo-Saxon community that leaves of the foxglove plant are useful in the treatment of dropsy (heart failure). From this knowledge came the discovery of the digitalis alkaloid and then of digoxin, followed by the identification of the digoxin receptor and then new-generation synthetic drugs that act on the receptor. Swaminathan's prescription will mean that a fraction of the IPR on the latest drugs will return to the Anglo-Saxon communities, but what then of the other intermediaries in the evolution of the invention?

It would appear, therefore, that the concept of limited-term monopoly followed by transfer of the knowledge to the public domain is an equally reasonable and a more workable solution. Consequently, an important corollary to my position is that India may adopt the patent protection mode even for conferring IPR on new plant varieties instead of considering alternative *sui generis* systems.

Finally, how would an IPR regime as the one argued for above affect the economy of India? I confess that I am not an expert to answer this question, and it is quite possible that our country should not adopt such a regime because it will be economically harmful for our countrymen. In that case, however, the economic justification for not adopting IPR for life forms should clearly be spelt out and the reasons why it will be disadvantageous for the country be cogently argued. Such a decision will then reflect economic realities, which will be used to con-

sciously override the scientific arguments presented here.

As indicated above, it may not be sufficient to make the case that patents in general are economically harmful and therefore that patents on life forms should be disallowed. One also runs the risk of being accused by other nations of being insensitive to the issues of promoting multilateral trade and hence of being subjected to sanctions, which may prove to be more economically ruinous in the long run. Thus, to exclude life forms from IPR on 'scientific grounds' will be an instance of using a false proxy to defend oneself in what is really a socio-economic disagreement between the world's trading nations.

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SCIENTIFIC CORRESPONDENCE

Polyamine biosynthetic pathway: A potential target for plant chemotherapy

The discovery of polyamines stemmed from the observations of crystals of a polyamine from human semen in 1678 by Antoni van Leeuwenhoek. Later in 1888, these crystals were identified as an organic base and given the name spermine¹. After a long gap, the reemphasis on polyamine perspectives in biology began in the 1960s and 1970s, with the accumulation of data on their role in cell proliferation and differentiation^{1,2}. However, this area of research has grown in significance in the last 10 years (especially from molecular biology) as these naturally occurring polycationic small ubiquitous molecules play a pivotal role in diverse cellular and molecular processes such as the regulation of cell division, growth and development, membrane stability, synthesis and function of DNA, RNA and proteins in many organisms, including plants³. It has been suggested that polyamines could be treated as a new class of 'intracellular growth regulators' or second messengers⁴. Although the

mechanism of action of polyamines in various cell functions is not clearly known, (especially in plants), the polyamine biosynthetic pathway is fairly well established³.

The most common polyamines are putrescine (diamine), spermidine (triamine) and spermine (tetraamine). Putrescine can be formed by two biosynthetic pathways, either directly from decarboxylation of L-ornithine by ornithine decarboxylase (ODC) or indirectly from L-arginine decarboxylation by arginine decarboxylase (ADC) through a couple of intermediates. Spermidine and spermine are synthesized by the addition of an aminopropyl group [donated by decarboxylated S-adenosylmethionine (SAM) formed from decarboxylation of SAM by SAM decarboxylase] to one or both primary amine group of putrescine by spermidine and spermine synthases, respectively¹. The specific inhibitors are available for the enzymes involved in polyamine biosynthesis⁵ (Figure 1). For

instance, difluoromethylornithine (DFMO) and difluoromethylarginine (DFMA) specifically and irreversibly inhibits ODC and ADC, respectively⁵. Both these pathways operate in plants and bacteria¹, but pathogenic fungi⁶⁻⁸, with a few exceptions^{9,10} and most probably protozoa¹¹ and insects¹² possess only an ODC pathway for polyamine biogenesis as in case of animals and humans¹³. Since a majority of fungi are dependent on ODC pathway for polyamine formation, which is an absolute requirement for normal fungal growth and development, the specific inhibition of fungal polyamine biosynthesis using ODC inhibitors like DFMO should be lethal¹⁴. In fact, this was the basis for the discovery of control of a plant disease by selective inhibition of fungal polyamine biosynthesis, without affecting polyamine biosynthesis, growth and development of the host plant as it contains an alternative ADC pathway for polyamine formation¹⁵. Previously, selective targeting of polyamine biosynthetic