Tropical mycology and biotechnology

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The relevance of tropical mycology to biotechnology rests on mycodiversity and the enormous fungal power that such mycodiversity implies. The strategies, techniques and priorities in harnessing fungal power for human needs are outlined. The author explains the urgent need for a fungal inventory of the tropics, for a combing of special microhabitats and ecological niches for mycogenomes, the maintenance in culture and conservation of these genomes and the study of their secondary metabolites and other attributes, and co-evolution with other genomes. These genomes are irreplaceable and must therefore be conserved.

> *Wild species in tropical forests and other natural habitats are among the most important resources available to humankind, and so far they are the least utilized.*
>
> *E. O. Wilson*

THE origins of biotechnology lie in man's intuitive skills and ingenuity in harnessing fungal and microbe power for human needs. But what is biotechnology? Is it the technology of using available biological material, the living biota, by domestication, to a purpose and an advantage? If so, what is agriculture? And, what is forestry? Or, is it the manipulation of biota at the molecular level, or application of genetic engineering to endow a living system with new but desirable attributes or abilities? In the broadest sense, yes—all this and, if this is true, biotechnology is not new. The making of wine, the production of ergot, the cultivation of edible mushrooms, and the cultivation of truffles are some classical examples.

In considering the origins of biotechnology, we cannot escape noting that there is the art of a biotechnologist and there is a science of biotechnology. Historically, biotechnology is an offshoot of the art of the biotechnologist. Indeed, the classical examples mentioned highlight man's early emergence as a biotechnologist. The more recent examples of harnessing fungal power for human needs highlight the massive potential and future possibilities in this vital area.

The basis of biotechnology

All biotechnology must start with a naturally occurring but preferred genome, an organism with known genetic potential. There is no other way. The process of identification of such a genome, then, is of the essence of good biotechnology. This involves the identification/location of a fungus active in a process in nature, and then its 'domestication'. The biological activity/activities of the fungus in nature are important. The uniqueness of fungi in being able to produce an unbelievably amazing variety and number of enzymes confers on them the ability to colonize and degrade a variety of substrates and also the potential to synthesize an extraordinary variety of metabolites with biological activity. There is possibly no substrate that the fungi cannot colonize and degrade: these include cellulose, hemicellulose, lignin, cutin, chitin, keratin and even biocides and toxic components of industrial effluents and wastes. The fungi are thus effective scavengers and, more important, play a significant role in recycling of nutrients and in geobiochemical processes in the biosphere. Their co-evolution with plants, animals and other biota is only beginning to be appreciated and there is much more that one can learn and benefit from the many mutualistic, antagonistic and synergistic interactions that are a unique feature of their biology. Anyone who wants to harness fungal power for human welfare through biotechnology should have a comprehension and appreciation of these.

Relevance of tropical mycology

Exploration

The relevance of tropical mycology to biotechnology rests on the remarkable biodiversity of fungal genomes extant in the tropics, despite the continuing destruction of valuable germplasm of plants, animals, fungi and other biota. The exploration of the fungus floras of the tropics and much of our present knowledge of these floras comes from the work of pioneers, like Saccardo, Spegazzini, von Hoehnel, the Sydows, father and son, Patouillard, Penzig, Butler, Lloyd, Petch, Koorders, van

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Overeem, Ciferri, Maire, Batista, Hansford, Boedijn, Heim, Mundkur, to name a few. The charting of fungus floras and the identification and description of fungi with which these pioneers were primarily concerned provide at most a partial inventory of the fungal genera and species of the tropics. More recent exploration and study have added considerably to our knowledge of tropical mycofloras.

Culture collections

It is furtunate that there was early in the development of mycology an appreciation of the need to study fungi in culture which began, in fact, with P. A. Micheli (who is deservedly honoured with a statue in Florence), but bloomed in the work of Anton de Bary and his illustrious student Oscar Brefeld on fungal polymorphism, and found fruition in the work of Pasteur on fermentation. It is in the wake of these that some of the earliest culture collections such as the Centraalbureau voor Schimmelcultures at Baarn in the Netherlands came to be established. Not surprisingly, culture collections are currently the primary sources of fungal cultures (and of fungal genomes) for use in biotechnology. But what do they hold? Though vast, they have mostly the common and the uniquitous moulds, Aspergilli, Penicillia, Fusaria and the like, though efforts are on to have unusual fungal species too. One must also note that these fungi in culture are not what they are in nature, but what they are not. This detracts from their utility in biotechnology.

Fungal secondary metabolites

Following the discovery of penicillin, a great many of these cultures have been screened by organic chemists or by the industry for metabolites of useful biological activity. Working at the London School of Tropical Medicine and Hygiene, Harald Raistrick reported, over a period of years, many novel secondary metabolites from mould species. Of the many secondary metabolites he isolated and described, only one, griseofulvin from *Penicillium griseofulvum*, turned out to be useful, in this case an antifungal antibiotic.

It is hardly possible to keep a count of secondary metabolites of fungi, but a list was provided by Turner in 1971. In presenting a further list twelve years later (1983), Turner and Aldridge wrote: "the number of secondary metabolites of known structure has more than doubled in the period. In *Fungal Metabolites II* we list nearly two thousand new metabolites". And yet, they add: "Apart from the β-lactams, which continue to be of great medical and commercial importance, the discovery of utility among the fungal secondary metabolites has been disappointing, especially since many possess biological activity. However, although the number of compounds isolated in the last 12 years is large in context, and the number of fungal preparations screened still larger, both are small compared to the number of compounds which must be tested before a new medicine is discovered." Admittedly, the vigorous hunt for new metabolites from fungi has not been sufficiently encouraging.

But, why? Consider the fungi that produce the β-lactams. The mould that settled on a petri plate in Fleming's laboratory in the hospital in Paddington in London, identified as *Penicillium notatum*, was described in 1912 by Westling in Sweden and this seemingly innocuous mould remained unnoticed until Fleming's discovery in 1928. The world's penicillin, however, does not come from this mould but from another *Penicillium* strain of *Penicillium chrysogenum* Thom from the Thom collection of Penicillia. And the Thom strain came from a decaying cantaloupe in the US! In the commercial production of the other β-lactam antibiotic cephalosporin, the original strain of *Cephalosporium* isolated by Brotzu from a sewage outfall off the Sardinian Coast in 1945 appears to be the one still in use. Unusual fungi lurk in unusual places. This further reinforces Turner and Aldridge's point about the need to screen a very much larger number of compounds, and hence of fungal genomes, than hitherto, for any success in the screening programme.

But where can we expect to find such compounds, especially hitherto unknown novelties, and the fungal genomes that would produce them? Not, perhaps, in culture collections from which we have drawn heavily and traditionally in the past, and which largely hold the common moulds, but in the patches of tropical forest, patches though they may be, in Southeast Asia and elsewhere, in peculiar and little explored special ecological niches, in microhabitats, and in remarkable associations of the most diverse kind. We must comb the niches, microhabitats and associations in the patches of tropical forest that still remain before they are completely wiped out and vanish from the planet by our own folly. We must screen fungi in unusual ecological niches and habitats for their activity.

A fungal inventory of the tropics

We need a fungal inventory of the tropics. There are supposedly about 69,000 described accepted species of fungi on a conservative global estimate. In his Presidential Address to the British Mycological Society, Hawksworth explained why this estimate is conservative and why one may expect a more accurate estimate from more intensive fungal exploration. Indeed, Hawksworth (in litt.) gives an estimate of global species as 1.5 million derived by extrapolations from three different data sets. The status of mycology in Southeast Asia was reviewed by mycologists from several countries at the Workshop on Progress in Applied Mycological Research in the Tropics held in Singapore in 1985 (see *Proceedings of the Indian Academy of Sciences* (*Plant Sciences*), 1986, **96**, 333–392). In an intensive study of microfungi of the Western Ghats including the Silent Valley, the author noted for each of the groups studied, viz. the Hyphomycetes (Deuteromycotina), the Coronophorales, the Diatrypaceae and the Diaporthaceae (all Ascomycotina), 8–37% of the genera, and 16–33% of the species were new, depending on the group. The author has presented detailed data elsewhere. These data are based on collections made in a dozen locations along the western ghats from Karwar in the north to Kalakadu in the south and so present a fairly reasonable picture of the diversity of the microfungal floras in areas hitherto not explored.

Vast areas in the tropics and elsewhere in the globe remain totally unexplored, and others only partially. Fungal exploration is restricted so far to locations where mycologists have collected, and then only to particular fungal groups that have received attention from taxonomists with expertise in these groups. That is why it is imperative that the major classes of the fungal kingdom are studied. A range of techniques need to be used for isolation, depending on substrate relationships and preferences of specific taxa. The use of suitable baits would facilitate isolation of fungi not appearing on the conventional dilution plate. John Karling, well known for his work on the lower fungi, used chitin, keratin and other baits and isolated many interesting chitinophilic and keratinophilic chytrids from Brazilian soils. Innovative techniques such as Warcup's soil-plate technique and his soil-steaming technique both broaden the variety of fungi isolated, the latter in a selective way by which interesting basidiomycetes and ascomycetes not appearing on dilution plates can now be isolated. Decades ago, Sparrow recorded several common and obiquitous moulds from deep sea mud using conventional techniques. Exciting though this report is, one wonders what other interesting or unusual moulds may lurk in the habitat. Again, a clear picture will emerge only from using a variety of isolation techniques and baits. In his Benefactor's Lecture to the British Mycological Society, Metzenberg speaks of ways in which molecular biology can help in the discovery of 'unculturable' fungi in soil and other complex habitats.

It would not suffice if fungi are thus collected and described, they must be brought into culture, though this may not be possible always. Systematic exploration in the tropics must concern itself with bringing into culture as many species as possible, apart from probing into their biology, their functional role in the ecosystem and their interactions with other biota as pathogens and parasites, or as symbionts, or as partners in coevolution. We need inventories of these. I shall explain this further with a few examples.

Fungi associated with insects. As an example of the success that comes from efforts in this direction we may cite the work of John Nathaniel Couch (1896–1986) on *Coelomomyces*, culminating in the publication of a monograph of this blastocladiaceous genus, species of which are pathogens of mosquito larvae in the tropics. Two new species of this genus were described on mosquito larvae from India many years ago by M. O. T. Iyengar. Quite interestingly, some species of *Coelomomyces* complete their life cycle on another unrelated host, the copepod, in aquatic environments in the tropics. We have thus a great corpus of data on the taxonomy, biology and distribution of this group of entomogenous fungi, chiefly from the work of Couch, which has potential use in the control of malaria through the biological control of mosquito larvae. There are also many other entomogenous fungi in the tropics as one may see from the classical studies of Roland Thaxter on the laboulbeniales, of Kobayasi on *Cordyceps* or of Petch on hypocreaceous and other entomogenous species, but here again many taxa await collection, identification and study. Then there are the fungi associated with termites and termite mounds, with ambrosia and bark beetles, with leaf-cutting ants, with scale insects (*Septobasidium*, *Tompetchia*) and the like. There are also many little-understood fungus–insect interactions in microhabitats such as wood and litter. Studies of these interactions and the fungi involved have implications in environmental quality, public health, and biotechnological options.

Fungi on plants. The inventory of fungi on plants calls for similar approaches. There have been numerous studies on fungi of the rhizosphere and rhizoplane of a range of crop plants. In a great many of these studies, hyaline or dark-coloured sterile fungi that are almost universally present on the rhizoplane of a range of plant species have been noted and reported by many students, but what they are and what they do in their typical microhabitat — the rhizoplane — is not known. These seemingly innocuous, uninteresting and apparently unidentifiable fungi have generally been ignored; they need to be investigated. The recent discovery, by Dewan and Sivasithamparam, of a sterile red fungus on root systems of wheat and ryegrass in Western Australia and of its potential in the biocontrol of take-all of wheat illustrates the point beautifully. Wood and bark of tropical tree species harbour fungal communities whose interactions between themselves and with their host/substrate are poorly understood. The study of these fungal communities *vis-à-vis* the host/substrate would be meaningful if one can obtain information on fungal metabolism *in situ*, especially production of metabolites. Though fungi are gregarious, and 'nature does not work with pure cultures', some fungal microhabitats are often exclusively colonized by single species and, in such cases, *in situ* identification, even isolation, by appropriate techniques, of the metabolites within the colonized substrate should be possible and would be pertinent to our objective.

I say this because, in the past, the study of metabolism of fungal pathogens of plants and of plants infected by fungal pathogens has thrown up discoveries which have become central to the biotechnology theme today. The discovery of the gibberellins, and of fusaric acid *et al.* are examples. Both are secondary metabolites of fusaria involved in plant disease. Currently, at least 57 kinds of gibberellins are known: 16 only from *Gibberella fujikuroi* (anamorph: *Fusarium moniliforme*), the fungus causing the bakanae disease of rice plants, 31 only from higher plants, and 10 from both sources. The ability for gibberellin biosynthesis so far known only in *Gibberella fujikuroi* among the fungi, has now been noted in *Sphaceloma manihoticola*, the fungus that causes the superelongation disease of cassava (=tapioca, *Manihot esculenta*), an observation that again highlights the point that many such biosynthetic abilities lurk in nature in fungal wild types and await discovery.

Relevant to this theme are also recent discoveries pertaining to fungal endophytes, for example, of the Gramineae in which infection may stimulate growth of the plant and concurrently build up toxins *in vivo* which may be inimical to animals or pests feeding on these grasses. That these infected grasses discourage herbivory in animals or ward off insects is now clear. The Balansiae and *Claviceps* spp. are the classical examples of fungal endophytes. The Balansiae comprise species in the genera *Atkinsonella*, *Balansia*, *Balansiopsis*, *Epichloë* and *Myriogenospora*. Other endophytes asymptomatically infecting grasses are species of *Acremonium* (Sect. *Albo-lanosa*) of which several are known. The curious thing about these is that some of them have not been cultured at all and when it has been possible to bring them into culture, they may not sporulate in culture, or else they do not produce a teleomorph. This reinforces the emphasis made already on the need to study sterile fungal forms from nature. There are yet possibilities of locating in the tropics grasses with other Clavicipitaceous or other endophytes. Insects feed less on, and do less damage to, grasses infected by endophytes. Naturally, these infected grasses may hold metabolites with insecticidal or insect-repellant properties. There have also been reports of toxicity of endophytes in conifer needles to insects. Indeed, discoveries of other fungal endophyte–plant systems can well be expected from future fungal exploration in the tropics and may have potential, for example, in biological control of insects.

Though some endophytes do not sporulate and, for that reason cannot be precisely identified, we must note that they yet have a metabolism, and that needs study. We should not underrate the functional role of sterile mycelial systems in nature or their metabolism. For obvious reasons, the sterile fungal component in tropical and other ecosystems has received no attention from even mycologists and, I believe, offers a potent source for biotechnology.

The composition of fungal communities on wood varies with the tree species and is characteristic for deciduous, conifer and other types. This is true of fungal successions also and the potential of the many fungal species colonizing and breaking down wood in forest ecosystems has not been appreciated or used appropriately in biotechnology. This applies to forest litter and mycoflora of litter in the tropics also.

The significance of fungal specificity. The tropics are known for the remarkable diversity of flora and fauna. Though many fungi are ubiquitous and have a global distribution, there are yet those that are fastidious in their choice of host/substrate. Interestingly, this is true even of saprophytic fungi. Thus, species of *Arthrinium*, *Pteroconium* and *Cordella* (all hyphomycetes) occur primarily on grasses and sedges, some specifically on bamboos in the tropics: the list of fungi on such monocots is virtually endless, but the point to note is that their occurrence worldwide is confined to these specific hosts/substrates of choice. Many other examples of substrate specificity of saprophytic fungi can be given but the essential point to note is that there is a link between choice of substrate/host and the metabolism of the fungus.

There is as yet no complete inventory of plant and insect species of the tropics, nor of the fungi associated with them. But we do know that two of the remarkably species-rich groups, the flowering plants and the insects, especially the arthropods, are dominant in tropical forests. Each species of plant, and often insect too, can harbour several fungal species synchronously or, frequently, in succession. It is then reasonable to expect an extraordinarily greater number of fungal species than there are, for example, plant species. The discovery of new or interesting fungal taxa from new hosts/substrates predictably means also the discovery of fungal genomes with unusual and novel biotechnological potential. Such new or interesting fungal taxa may have unusual features in morphology and developmental morphology such as, for example, what was reported for a new hyphomycete with basauxic conidiophores described by the author recently on *Xanthorrhoea preissii* Endl. from western Australia. [Species of *Xanthorrhoea* (Xanthorrhoeaceae) are endemic to Australia and are not known from any other part of the world.] This may be appreciated by the fungal taxonomist; but those like me who believe form and function are closely linked cannot but see in these morphological or taxonomic novelties, functional and metabolic novelty of relevance to biotechnology. In contrast, a great many fungal species from which secondary metabolites have been obtained belong to one or the other groups of phialidic hyphomycetes currently recognized by the author largely on the basis of developmental morphology.

Freshwater, estuarine and marine mycota. Fungi in aquatic ecosystems, freshwater and marine, have received relatively less attention than fungi in terrestrial ecosystems. Freshwater fungal components are represented chiefly by the Chytridiomycetes and the Oomycetes, especially the Chytridiales (chytrids) and the Saprolegniaceae (water moulds). Some of these are amphibian — theoretically on the road to colonizing land from water — and may cause disease in plants. Ingoldian fungi, the aquatic hyphomycetes, are components of freshwater litter throughout the world, and are doubtless involved in the decomposition of freshwater litter. New and interesting taxa of Ingoldian fungi are continually being described, especially from the tropics, but again we have not tapped this source for biotechnology.

Fungi are a major component of marine biota as well. Marine wood harbours a diversity of species of Ascomycotina and of conidial fungi which are again involved in decomposition of this substrate in the marine environment. There are also members of the Mastigomycotina, though not in a measure comparable to that in freshwater. The sea is also the home of some special and intriguing groups such as the Thraustochytrids. Thraustochytrids have been reported from the North Sea, interestingly also from tropical mangrove ecosystems. Since the publication of the first ever major paper on marine fungi in 1944 by Barghoorn and Linder, there has been much interest in them, but their inventory has only begun. Though there is awareness of the importance of studying the physiology and biochemistry of these organisms, their biology and their interactions with other biota in the sea require intensive study. The current interest in marine fungal biota as vital sources of bioactive compounds must penetrate deeper and concentrate on the taxonomy and biology of marine mycota, particularly on thraustochytrids and the like, for example in the mangrove or coral reef ecosystems of the tropics. This is uncharted sea for the biotechnological navigator.

Ethnomycology. Primitive tribes and ethnic peoples in many parts of the globe, especially in the tropics, live in a world of their own and are perhaps the only humankind who still practise the art of the biotechnologist which I mentioned in the beginning. Their use of fungal remedies for disease, of fungal food and of fungal hallucinogens is well documented in some cases and reveals the uncanny intuition and extraordinary skills of these tribes and peoples in their understanding and comprehension of the distribution, nature and use of the fungi of their choice. For example, the use of the fly-agaric (*Amanita muscaria*) by the Siberian Koryaks and Chukchis reflects their remarkable intuitive insight and understanding in using the fungus collected in the wild for hallucinatory purposes effectively and economically. That the fly-agaric is most effective when taken in the dried form, and the bioactive metabolites are excreted in the urine were known to these tribes long ago. Work on the chemistry of the hallucinogens of *Amanita muscaria* and on the biochemistry of their metabolism following ingestion by man has served to confirm the beauty of the art of the Koryaks and the Chukchis. The rise of the subdisciplines, ethnobotany, ethnomycology and ethnopharmacology symbolizes the many benefits that one might derive from much valuable information that currently rests with tribes and primitive peoples in many parts of the tropics. The secrets of tribal art relevant to medicine and biotechnology in particular need to be probed into and documented before such information is totally lost.

The priorities

Having noted the relevance of tropical mycology to biotechnology, let us now list the priorities:

1. The mapping of our enormous and rich fungal resources is urgent, in view of the continuing degradation and denudation of tropical forests throughout the globe. We need an inventory of the fungal taxa — species, genera, families.

This can only be achieved by strengthening systematic capability — for fungi, plants, animals and other biota — and so needs to be given utmost priority. The IUBS initiative in launching a programme for 'Improving the Stability of Biological Nomenclature' will strengthen the bases of systematics, which is so vital for progress in science and in biotechnology.

2. There are many tropical habitats, associations, microhabitats and niches with fungi — saprophytes, parasites, symbionts — representing an extraordinary diversity in behaviour and metabolism. They need to be brought into culture, identified and studied.

Microhabitats and ecological niches hitherto neglected (mangroves, coral reefs and other saline microhabitats, bird sanctuaries, termite mounds, freshwater and terrestrial litter, etc.) and special biological groups of fungi (thermophiles, coprophilous, entomogenous, predacious, lignicolous, etc.) need to be combed vigorously.

A wide variety of innovative techniques and a variety of baits need to be used for isolation.

3. Not merely their taxonomy, but understanding of their biology and functional aspects of *their metabolism in their natural habitat* would help unravel their potential use in biotechnology.

4. Mycodiversity implies functional and metabolic diversity, a diversity in enzyme systems. Secondary metabolism and metabolites of the many novelties that abound in microhabitats, naturally, need to be taken up for study on a war footing.

5. Interesting or intriguing fungal groups and taxa, neglected so far, must be taken up for intensive study.

Conclusion

As I said in the beginning, all fungal biotechnology must begin with a preferred fungal genome drawn from nature—a natural species and its numerous genetic strains—with known genetic potential. There is no other way. That genome, and countless such other genomes represented in wild types in nature, are the repositories of whatever attribute or attributes the biotechnologist is looking for. There is little doubt that much can be gained from genetic manipulation of fungi (or for that matter of other biota) at the molecular level. This is generally appreciated. And it is good this is so. But what is generally not appreciated is the fact that the genomes for manipulation *must* come from the mycodiversity extant in the biosphere. The enumeration, identification, isolation, maintenance in culture, and conservation of these genomes in the biosphere is therefore the most urgent and vital single task for mycologists, biotechnologists, biologists, naturalists, environmentalists or whatever one may like to call oneself—but essentially for Man, and for Science. A culture collection of tropical fungi needs to be built up. Concurrently, our knowledge of their genetics, physiology and biochemistry must be strengthened by intensive study. The crisis before us is the threat of annihilation of our vast and valuable fungal resources which are irreplaceable. We have a challenge here and we shall not let it pass. Mycologists in Asia and in the Tropics have a major role to play in this, but its impact will be global.

The selected references given below are supportive of the general theme of the lecture and provide detailed information on the points and ideas discussed.

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