# GAMES THAT GENES PLAY: HOST-PARASITE INTERACTIONS IN A GAME-THEORETIC CONTEXT

David J. Rapport[1] and Clayton O. Person[2]

Received January 21, 1979; October 17, 1979

ABSTRACT: The genetics of the flax (*Linum usitatissimum*) and its parasite, flax rust (*Melampsora lini*) are described within a game-theoretic context. Endless genetic cycling occurs if one postulates that the cost of the host or parasite of carrying ineffective genes is sufficient for certain substitutions. Basic genetic rules for this host/parasite interaction include: (1) The development of Resistance at any host locus for which the parasite does not possess the corresponding virulent gene is sufficient to act as a stop signal and prevent parasite development. (2) It is to the host's advantage to expand the number of R-genes, since the advantage to the parasite decreases with increasing number of gene-gene interactions. (3) The fitness of a pathogen genotype is a function of both its need when the pathogen interacts successfully with the host and on the proportion of total successful interactions. (4) For parasites with two or more unneeded virulence genes its reproductivity is reduced. The game theoretic description of this host/parasite interaction suggests explanations for the genetic structure of this system and poses a number of questions for further research.

* * *

Games, decisions, and evolutionary processes are interrelated in various ways. Evolutionary processes can be described in terms of games, and game strategy, and strategies in managing our natural resource might profit from this knowledge. Of course, the question arises: How much do we really know about the nature of evolutionary games, and is our knowledge sufficient to interfere with nature with any degree of confidence? There have been suggestions made recently, for example, by Rene Dubos, that we ought to be able to do better than nature. He suggests that we ought to be able to restructure "natural" communities, which would be much more pleasing to man from an aesthetic point of view, from his needs for materials, and perhaps from certain long-term viability and stability points of view. There have been suggestions by others that once the rules of assembly of species groups are understood, we ought to be able to construct new kinds of communities that will increase biological diversity world-wide and, by implication, guarantee more stable, resilient natural systems.

One might assume that these kinds of proposal rest on a fairly sophisticated (at least intuitive) understanding of the "evolutionary" games and their implications for the manipulation of ecological structures to man's benefit. Unfortunately, there are considerable doubts, at least in my mind, that this is actually the case. To be sure, we have very lucid discussions of some of the general features of evolutionary games. I refer here to Lewontin's paper (1961) introducing some of the formalisms of game theory in

* * *

[1]Department of Zoology, University of Toronto, Toronto, Ontario M5S 1A4

[2]Department of Botany, The University of British Columbia, Vancouver, British Columbia V6T 1W5

* * * * * * * * *

Evolutionary Theory 4: 275-287 (July, 1980)

a biological context, and to the extensive reviews of the applications of game theory in biology by Slobodkin and Rapoport (1974). These and other contributions (Rapoport, 1956; Slobodkin, 1964) have outlined general considerations in the application of game theory to evolution. But it may be a rather large step to move from general theoretical constructs to an understanding of particular biological interactions. some of the difficulties that might be encountered are of the following kinds:

(1) The approach of game theorists may lead to the temptation to impose a priori, a game-theoretic model upon nature, rather than deducing the features of the game from a careful study of the phenomenology. Of course pure empiricism is neither possible nor all that insightful. One is reminded here of Haldane's reply to the question of what might be inferred about the Creator from the Creation. Haldane reportedly quipped that the Creator was obviously very fond of beetles!

(2) Identification of the players, a specification of the "rules" of the game (e.g. the constraints and "moves" that are open to players), the identification of a well defined preference for each player among the possible outcomes in the evolutions context are required. As Rapoport and Slobodkin have pointed out in this symposium and elsewhere (Slobodkin and Rapoport, 1974), the evolutionary game differes in at least one important aspect from standard games---that is the winnings are not in terms of stakes that can be "cashed in" but rather in terms of continued existence for the species. Evolution viewed as an "existential" game, brings to the fore the problem of evaluating moves in terms of probabilities of extinction during a specified time period.

(3) The large number of players in an evolutionary game often exceeds the limitations of formal two-player or three-player games. Three-player games already introduce considerable complexities, and as is well known many biological situations might not readily be comprehended unless a relatively large number of species interactions were taken into account. Consider for example the community of phytoplankton or zooplankton and the various strategies that species in these groups evolved in response to changes in seasonal availability of resources. Or consider the highly interactive population dynamics involving the forest insect pest, the spruce budworm, its associated coniferous host species (black spruce and balsam fir) and the white birch.

To be manageable in a game-theoretic context, the complexities of biological interactions must be simplified. Just as Franklin and Lewontin (1970) devised collapsing rules so that the entire chromosome might be treated as a functional unit (rather than individual "genes"), the number of actors in the evolutionary game often needs to be compressed into manageable groupings.

(4) What are the constraints ("rules") on "moves" that the players can make in evolutionary time. At the phenotypic level, the diversity of life forms, and their behavioral plasticity is convincing evidence that there appears few easily identified constraints, except those of thermodynamics, and to some extent a species' evolutionary history.

(5) How does one account for changes in the "rules" of the evolutionary game as the game proceeds? (By "rules" we refer to the allowable transformations, behaviors etc.) For example, the rates of mutation and kinds of mutations are under genetic control in some systems. This control itself can

change in response to selective pressures in the course of evolution. The rates of mutation are also under environmental influences which change over time. The rates of recombination which give species the possibility of making new moves also appear, in some systems, to be under genetic control, as, for example, in *Drosophila*, where there are certain chromosome inversions which seem to reduce the possibilities for obtaining new genetic combinations; and in the plant, *Oenothera*, there are certain ring structures of chromosomes which also may tend to reduce the possibilities for evolving new combinations.

The challenges to game theorists working in evolutionary theory are many. An obvious "strategy" is to identify a problem in which these complexities are minimized, and then develop sufficient biological understanding of the underlying processes that areas where game theory may make contributions towards biological understanding may be identified. This paper serves largely a heuristic function, consistent with these goals. We describe the strategies (of the genes) which appear to govern the host-parasite interactions of flax and its associated rust, and may be characteristic of other interactions in this class (e.g. wheat and wheat rust, for example). We attempt to formulate the description in a game-theoretic context and pose some questions which we hope might interest game theorists to work on this challenging system.

## FLAX-RUST INTERACTIONS: THE GENE FOR GENE HYPOTHESIS

The genetics of flax (*Linum usitatissimum*) and its parasite, flax rust (*Melampsora lini*) have been the focus of considerable study over the last several decades. The seminal work of Flor (1956) elucidated the basic strategies involved in interactions between these "players"; namely that the host appears to utilize exclusively a multiple allelic system (operating at a limited number of loci) while the parasite possesses a multiple loci system, potentially capable of expressing all of its virulence at one time.

When the flax and flax rust come into contact in nature, two basic outcomes occur: either there is an extensive disease development (designated "+" in Figs. 1 and 2) in the host, or there isn't. The "+" disease reaction caused by the flax rust involves the formation of pustules on the leaves of the flax plant, which serve as foci for rust reproduction. The details of the phenomenology here are not of interest here. It suffices for our purpose to classify plants by whether or not they are susceptible to the parasite.

In Figure 1a, the four possible outcomes are shown in a highly simplified game matrix. Hosts are either susceptible or resistant. Parasites are also of two types--avirulent or virulent. If the host is susceptible, contact with flax rust will always result in a disease reaction, reducing host viability and host capabilities to reproduce.

However, when a resistant host encounters the same parasite it will not succumb to a disease reaction if the parasite is of the avirulent type (X), but it will if the parasite is of the virulent type (Y). Thus, virulence and avirulence are not defined independently of susceptibility and resistance.

As one can see from Figure 1a, there are only two possible outcomes when host meets parasite.

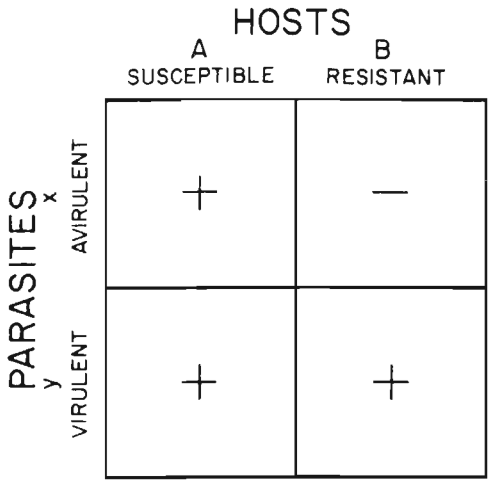


Figure 1a.: Host-parasite interactions. A disease response is indicated by +.

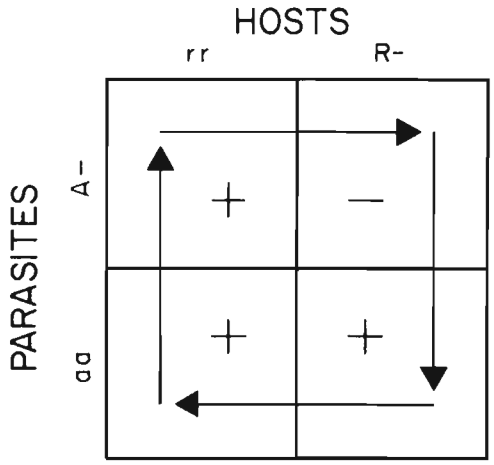


Figure 1b.: Gene-for-Gene hypothesis. Genetic cycling occurs provided non-effective (higher cost) R genes are replaced by r, and unneeded aa genes are replaced by lower cost AA.

As shown in the diagram, there is only one situation in which the host escapes a disease reaction, that is when it is of resistant type and meets a parasite of an avirulent form.

Now, to translate this description at the phenotypic level to the underlying genetics, consider the example shown in Figure 1b. In this single locus model, both host and parasite are represented by two alleles at a single locus. The parasite avirulent form is represented by (A), which is dominant and

therefore needs expression at only one of the homologous sites to be effective. Similarly, host resistance (R), is also dominant. Thus, so long as the host contains at least one resistant allele (R), and the parasite at least one avirulent allele (A), the host escapes a disease reaction. We note that the gene-for-gene hypothesis of Person (1966) (see also Person and Ebba, 1975; Groth and Person 1976; Person et al, 1976; Sidhu, 1975) applies to the entire matrix, not simply the single case where no disease reaction occurs. Obviously, it is essential to view the complete possibilities, if only to recognize that one is considering a real host/parasite system! Unless a + reaction is possible, there is no indication that the host and parasite recognize one another as such.

The phenotypic virulence of the parasite is, of course, dependent on the genotype of the host. Any parasite is virulent if in contact with a susceptible host (rr), but only parasites (aa) are virulent in contact with all host genotypes including those that are R-. This means that the same parasite (A-) is virulent when in contact with host (rr) but avirulent when in contact with host (R-).

Consider the following sequence:

| | | Genotype | |
|---|---|---|---|
| | | Host | Parasite |
| Step 1: | Host susceptible; parasite virulent | rr | AA |
| Step 2: | Host resistant; parasite avirulent | RR | AA |
| Step 3: | Host susceptible; parasite virulent | RR | aa |
| Step 4: | Host susceptible; parasite virulent | rr | aa |

The above sequence which is more conveniently expressed in game theoretic matrix of the simple type shown in Figure 1b represents a game of endless genetic cycling. In game theoretic terms, there is no stable node. While it is relatively easy to justify (on the basis of standard neo-Darwinistic logic) the sequence of moves from Step 1 to 2 to 3, the move from step 3 to 4 and back to 1 again requires assumptions as to the cost to the host or parasite of carrying ineffective genes. The postulate that the resistant genome (R-) in the host is replaced by rr when the host population is heavily diseased (step 3 to 4) is based on the assumption of some additional cost to the host of maintaining alleles R over allel r when R genes are ineffective. This cost can be justified when R is effective in preventing disease reactions (e.g. the parasite is A-, but cannot be justified (in terms of a natural selection calculus) when the parasite is aa, since then the parasite is virulent regardless of the genome of the host. The postulated step from 4 back to 1 is easier to justify, since once the host is fully susceptible, the parasite is effective with either genotype, and according to van der Plank (1963, 1968) there is some evidence to suggest that stabilizing selection operates against virulence genes that are no longer needed.

The number of cells in a game matrix undergoes rapid expansion when the multiple allelic system of the flax host is represented more completely.

selective advantage of multiple alleles is obvious once it is recognized that the host is protected from the parasite if it contains a single resistant gene for which the parasite does not contain the double recessive virulent genome. Since the host that is $R^1$ $R^2$ is immune to all parasites except $a^1a^1a^2a^2$, the host is better off than a host homozygous for either resistant gene alone. In Figure 2, monocultures (most cereal crops, for example) easily succumb to a disease problem whenever the parasite is $a^1a^1A^2-$ if the host is $R^1R^1$ and also succumbes to $A^1-a^2a^2$ if the host is $R^2R^2$.

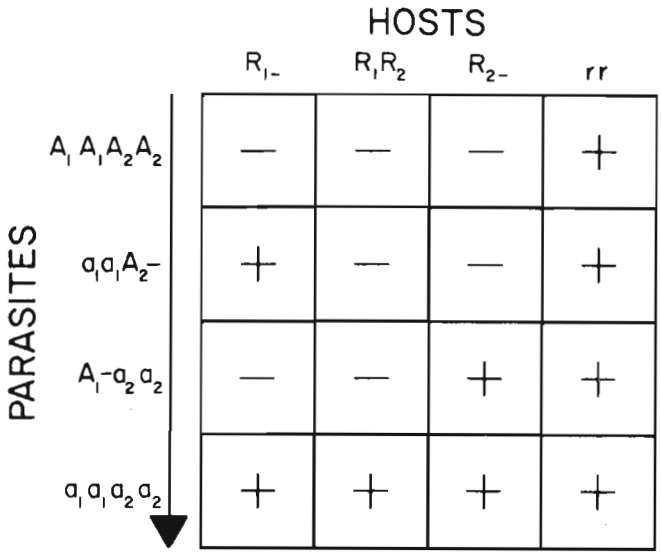


Figure 2.: Multiple alleles-single locus gene-for-gene interactions. Arrow indicates the direction of selection. Genetic cycling occurs if once the host population is relatively susceptible, the virulent genes of the parasite are replaced by the avirulent forms.

However, should the host contain both resistant alleles ($R^1R^2$) then its probability of a disease reaction is reduced to one-half, since the only effective parasite genome (e.g. virulent parasite) is $a^1a^1a^2a^2$.

To expand the model, consider the genetic cycling effect when it is assumed that the host population contains five alleles for resistance at the same locus, (Person, 1966). (Obviously an individual can contain only two of these resistant genes at one time at a single locus.) In Figure 3 the dynamics of the frequency of resistant genes is shown as the host population substitutes the most effective resistant gene for the least effective, keeping one move ahead of the parasite population which is also undergoing selection for the frequency of expression of virulence in its multiple locus systems.

In each step of the model (Figure 3) the host goes from initial resistance to susceptibility which sets up selection pressures to regain resistance by substituting a more effective gene for resistance for the least effective gene.

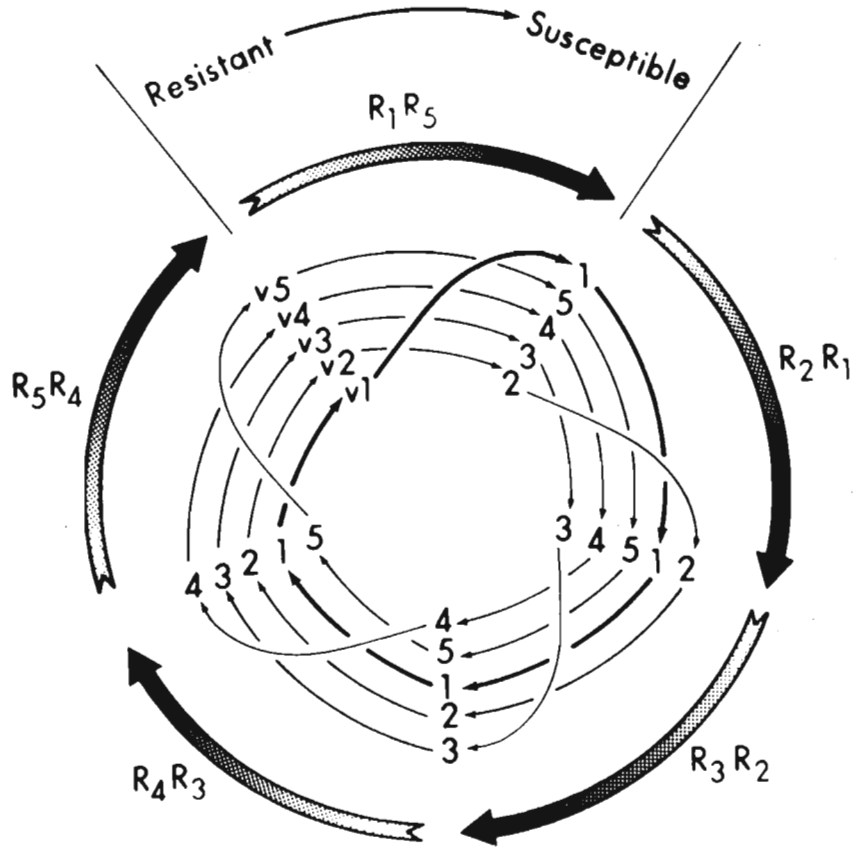


Figure 3.: Genetic cycling in host and parasite. Reproduced with permission from Nature. (Person, 1966).

For example, the host makes the move $R^1R^5$ to $R^1R^2$ when the parasite population contains $a^5a^5$ in high frequency and $a^2a^2$ in relatively lower frequency.

One can see the large number of moves now open to host and parasite as the system is expanded. For example, just considering the five alleles single locus system described above, there are $2^n \left(\frac{n\,(n-1)}{2} + n\right)$ interactions or 480 The possibilities expand multifold when multiple loci are considered for the host.

It is not known what limits there are for multiple loci, multiple allelic systems in the host. Flor (1971) described five loci, most of which were multiple allelic. However his analysis was based on the genetics from strains taken from widely dispersed locations (including Argentina, Europe, and Eurasia). The genes he has identified therefore exist as part of a number of separate host/parasite systems, and it is unlikely that these genes would be found as an integral part of a single host/parasite system.

GENETIC RULES OF THE GAME

From the description of the genetic interactions of host/parasite complexes, the following rules and genetic strategies appear relevant:

(i) If we regard the R:A interaction as a stop signal, then a single R:A interaction is all that is needed to prevent parasite development, and thus to ensure host resistance. The basic set of interactions, for each and every one of the gene-for-gene (G-G) relationships that may be operating in the system, is shown in Figure 1. For a complex system containing n G-G relationships, all of them have to be "+" in order for the parasite to succeed. If, at any one of these, the interaction is "-" (A:R), the parasite is stopped. This rule applies whether the G-G interactions involve R-genes that are allelic or whether they are at separate loci (non-allelic).

(ii) It is to the host's advantage to expand the number of R-genes. For a system in which there is a single G-G relationship, three of the four possible interactions favour the parasite. With 2 G-G relationships, the fraction is 9 out of 16. In general, where there are n G-G relationships, $(3/4)^n$ of total interactions favour the parasite. It is obvious that the advantage to the parasite decreases with increasing n.

The mechanism by which new R-genes are added to the system is interesting: Basically, an R-gene that is entirely new to the system will act as a "stop signal" for all parasites that are, at that time, part of the system. The new (mutant) R-gene is immediately advantageous, regardless of the genotype in which it has occurred. It will be incorporated into the system. (But, of course, the magnitude of the long term advantage will diminish as the system becomes larger.)

(iii) The fitness of a pathogen genotype (or of a pathogen a-gene) is a function of: (a) whether this gene is "needed" when the pathogen interacts successfully with the host; and (b) if needed, on the proportion of total successful interactions in which it actually functions as a needed a-gene.

Genes A and a can function in either of two environments (i.e., each can interact with either rr or R- hosts). Because gene a is a rare gene, we assume that the fitness of A ($=W_A$) is greater than that of a ($=W_a$) when virtually all hosts are susceptible. Were this not so, the R-gene introduced at step 2 would be ineffective. Thus, on rr hosts, we are safe (we think) in assuming that $W_A > W_a$. Now, on R- hosts, where A- is obviously "stopped", genotype aa succeeds. The critical situation is whether $W_a$ on R- hosts is greater than $W_a$ on rr hosts. The data are not conclusive. But, if van der Plank is right, genotype aa should have greater fitness on R- hosts (where a functions as a "needed" gene) than on rr hosts (where it does not). Let us assume that the fitness of aa on R- hosts is the same as that of A- on rr hosts. Now, for a mixed host population in which m represents the proportion of total interactions that take place on susceptible hosts, the change in relative fitnesses (of A and a) with changing proportions of m is given in Figure 4.

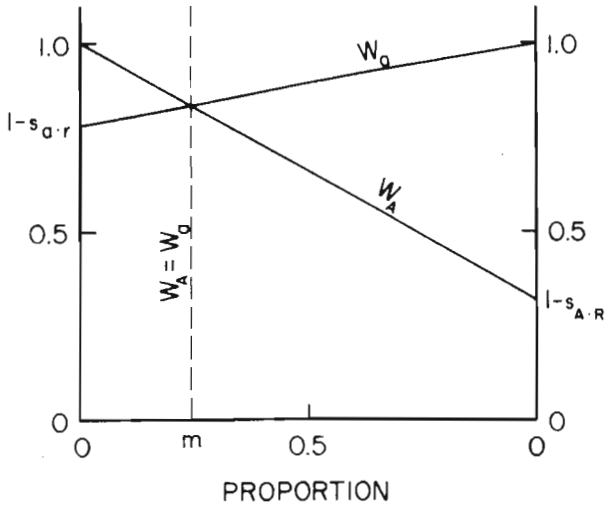


Figure 4.: Relative fitness of host and parasite. m= proportion of total interactions taking place on susceptible hosts. $s_a$ is the selection coefficient for the virulent gene in an environment in which they are not needed. Thus in an environment in which all interactions occur on susceptible hosts, the fitness of the virulence gene a is $1-s_{a.r}$. A similar argument is advanced for the fitness of the avirulent genotype in an environment in which all interactions take place on resistant hosts.

There is one value of m ($\hat{m}$) for which fitnesses of A and a are equal. (Figure 4) If m is made larger than this value, WA>Wa and the selective replacement of A by a does not take place. The message: R-genes need not elicit a selective process that brings forward related a-genes, providing that they are used judiciously. If one could actually measure the relative fitnesses of A and a in the two environments (i.e., on rr and R hosts), it would be possible (in theory) to determine the fraction m that should not be exceeded when an R-gene is used.

(iv) The fitness of a resistant host (or R-gene) is probably, as already mentioned, dependent on whether or not the R-gene in question functions as a needed R-gene. For a micro-evolutionary "game", in which there is no human interference, it would probably be important for hosts to have just the right number of R-genes.

(v) For parasites with two or more unneeded a-genes, the expectation (not as yet supported by experimental data, but reasonable) is that reproductivity will be progressively reduced. This kind of situation is normally handled (by theorists of population genetics) by assuming that the fitness losses are multiplicative. Thus, if fitness of a race with one unneeded a-gene is set at 1-s, then fitness of the race with two unneeded genes becomes $(1-s)^2 = 1 - 2\,s + s^2$.

## GAME THEORETIC ASPECTS OF HOST/PARASITE INTERACTIONS

The description of the genetic interactions in the flax and flax rust system suggest the following questions which may be amenable to a more formal game theoretic analysis:

1. Is the multiple allelic, multiple loci genetic system of the host, combined with dominance of resistant genes, coevolved with the recessive virulence of the parasite to prevent the parasite from becoming too successful and eliminating its host? That is, is this system a stable one, in that the parasite can't become too successful? Under what conditions might this stability break down?

2. Under what conditions does it pay the host and parasite to form a coalition (e.g. involving some host damage) to reduce the attractiveness of the host to potential harvesters (including man)?

3. What might be the strategies developed by man attempting to maximize his harvest of the host? Under what conditions would mixed cultivars be preferred to temporal changing the genetic stocks of the host? Would a mixed strategy of temporal and spacial mixing of the genetic strains of the host always be preferable to a pure strategy? Is keeping the percentage of resistant genes below the critical percentage for which selection for the countervailing alleles in the parasite becomes positive, an optional strategy?

4. Given the assumed higher cost of maintaining the resistance alleles in the host, do populations that grow in heterogeneous environments in which contact by the parasite is made more difficult, carry a lower optimum number of resistance genes? (e.g. is there a trade-off between a "strategy" of hiding from the parasite and being resistant to it?)

5. What is the optimal distribution of resistant genes in the host among loci and alleles? Does this strategy depend on the virulence and number of loci involved in the parasite?

6. What are the conditions that may favor an evolution from one form of association of host-parasite to another? That is what conditions might result in transformations between relations of parasitism, mutualism and commensalism? One is reminded here of the hypothesis that the mitochondria was at one time an endoparasite of a eucaryotic cell.

## ACKNOWLEDGEMENTS

We thank Anatol Rapoport and Ellie Rapport for their comments on an earlier draft of this paper. We thank Rodger Hansell for providing the initial stimulus to prepare this paper for the symposium.

REFERENCES

Flor, H.H., 1956. The Complementary Genic Systems in Flax and Flax Rust. Advances in Genetics. 8:29-54.

Flor, H.H., 1971. Current Status of the Gene-for-gene Concept. Annual Review Phytopathology 9:275-296.

Franklin, I., and R.C. Lewontin. 1970. Is the gene the unit of selection? Genetics 65:707-34.

Groth, J.V., and Person, C.O., 1976. Genetic Interdependence of Host and Parasite in Epidemics. Annals New York Acadamy of Science 97-106.

Lewontin, R.C., 1961. Evolution and the Theory of Games. Journal of Theoretical Biology. 1:382-403.

Person, C.O., 1966. Genetic Polymorphism in Parasitic Systems. Nature 212:266-267.

Person, C.O., and Ebba, T., 1975. Genetics of Fungal Pathogens. Genetics 79:397-408.

Person, C.O., Groth, J.V., and Mylyk, O.M., 1976. Genetic Change in Host-Parasite Populations. Annual Review of Phytopathology. 14:177-188.

Rapoport, A., 1956. Some Game Theoretic Aspects of Parasitism and Symbiosis. Bulletin of Mathematical Biophysics. 18:15-30.

Sidhu, G.S., 1975. Gene-for-gene Relationships in Plant Parasitics Systems. Science Progress, Oxford. 62:467-485.

Slobodkin, L.B., 1964. The Strategy of Evolution. American Scientist. 52: 342-357.

Slobodkin, L.B., and Rapoport, A., 1974. An optimal Strategy of Evolution. Quarterly Review of Biology. 49:181-200.

van der Plank, J.E., 1963. Plant Diseases: Epidemics and Control. Academic Press, Inc., New York, London. 349 pp.

van der Plank, J.E., 1968. Disease Resistance in Plants. Academic Press, Inc., New York, London. 206 pp.

OPEN DISCUSSION

Roger Hansell: In what sense do the rules of the game change?
Rapport: If we take the rules as constraints and one of the constraints, for example, is how fast can a move be made. That itself is under evolutionary control, under genetic control, and that itself is selected in the course of evolution. That's an example of a rule change or a constraint change in the course of the evolutionary game.

Lawrence Slobodkin, State University of New York, Stony Brook: I think there's a distinction between the rules of a game and whether you win it or not. I think I pointed this out once before. Obviously, if you're playing checkers you play by the same rules throughout the game. The constraints on your game change as the game develops, as pieces are lost and as the other player moves. It might be a valuable distinction to retain. If we consider the rules as given by the biochemist, the organism is playing by the rules as long as it's alive. Its probability of winning the game, or losing the game, changes with constraints. Would that be fair?

Rapport: I find quite a bit of difficulty in pinning down what the rules in the evolutionary game are. That's one thing I would want to think about.

Anatol Rapoport: Rules mean just this-- if the game is played in an extensive form, that is, from position to position in the course of time, then at each point where there is a choice the rules specify just what these choices are. Moreover, if we talk of game theory there must be some termination rule which specifies that at a certain position the game ends. Then, and only then, are payoffs apportioned, depending on which position ends the game. These payoffs are also part of the game. So the rules specify first of all who is to move, what the choices are that the player has at that position, and moreover the termination of the game, when the chips are cashed in and how much the chips are worth. Those are the rules. Now, if you mean that these rules change-- there are millions of evolutionary substitutions that can be put down to changes in the rules: for example, the environment changes.

David Rapport: Yes, the options or the selective pressures, what moves are most likely, would be changing and this is one thing. I don't know whether this is fair, but let's suppose we take a bacterial system in which initially there is high selective pressure for rapid reproductive rates because there are a lot of resources. Then in the course of building up the population there becomes a high selective pressure because now the population relative to the resources makes resources ver scarce; there is a high selective pressure for using resources very efficiently. Can that be considered a change in the rules of the game?

Anatol Rapoport: The difficulty is that you do not specify where the end of the game is. If you specify where the end of the game is then the game is played over again in a new environment and the payoffs may be different for a new position, if that's what you mean. But it's difficult to pin it down unless you specify just when the game ends.

David Rapport: The game ends for a player when it becomes extinct.

Slobodkin: Which brings you back to the set of properties of being alive as being the rules.

Anatol Rapoport: In other words, the only payoffs are being extinct or alive-- are those the only payoffs? There's a distinction there: if those are the only payoffs then natural selection in the sense of increasing or decreasing the probability of extinction at some future date is not included in the payoffs, and we would like to see that included in the payoffs.

Question: In the specific example given of the flax and the parasite, the change in the game strategy would depend on whether both are trying to survive. If both are trying to survive, following your circle, at each step it would be optimal for both to have a proportion of the population resistant to virulent alleles in such a way that both the parasite and the host can survive. Obviously, if the host quits, the parasite would also lose because the parasite cannot live without the host. It is possible that evolution, nature, would really favor a point of equilibrium while this struggle is going on, so then both sets of genes, the resistent genes and the susceptible ones, stay in an equilibrium position-- neither of the organisms lose out in the sense that the other one is wiped out.

David Rapport: Right. I think that's true of any strongly interacting system, whether it's a host/parasite or various predator/prey systems. Obviously, if it works out that one becomes too successful, the success sets up selection for less success if the thing is to remain a going game. I think that it's relevant too that in this particular game the host can survive without the parasite; if the parasite wants to keep in the game it can't be too successful and eliminate the host. I think you have this kind of consideration in a lot of predator/prey or host/parasite kinds of games. It comes back to specifying the utility function, which gets back to Professor Rapoport's point: the probabilities of surviving or staying in the game enter into it.
Question: What is a utility function?
David Rapport: A utility function in this sense is in terms of some sort of a payoff, which in this case is the probability of staying in the game.
Leigh Van Valen: We're talking about game theory and evolutionary theory, and at least evolutionary theory is in itself in an evolving state. I hope the same will be true for game theory, because it may well be the case that game theory as it now exists is not directly applicable to the evolutionary process, and we may be interested in how each theory may appropriately be modified in the context of the other.
David Rapport: I think this is a plea also for some sort of emphasis on an empirical approach, to looking at what nature DOES rather than imposing the game-theoretic structure upon nature, to try to derive from evolutionary experiences some of its rules: let nature tell you what it does rather than to impose the rules on nature.
Question: It seems to me that empirically the best parasites are the ones that make themselves necessary, so that that would be an additional point of strategy.
David Rapport: The parasite arriving at a mutualistic relationship?