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PERSPECTIVE

Social selection and the evolution of cooperative groups: The example of the cellular slime moulds†

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In social selection the phenotype of an individual depends on its own genotype as well as on the phenotypes, and so genotypes, of other individuals. This makes it impossible to associate an invariant phenotype with a genotype: the social context is crucial. Descriptions of metazoan development, which often is viewed as the acme of cooperative social behaviour, ignore or downplay this fact. The implicit justification for doing so is based on a group-selectionist point of view. Namely, embryos are clones, therefore all cells have the same evolutionary interest, and the visible differences between cells result from a common strategy. The reasoning is flawed, because phenotypic heterogeneity within groups can result from contingent choices made by cells from a flexible repertoire as in multicellular development. What makes that possible is phenotypic plasticity, namely the ability of a genotype to exhibit different phenotypes. However, co-operative social behaviour with division of labour requires that different phenotypes interact appropriately, not that they belong to the same genotype, or have overlapping genetic interests. We sketch a possible route to the evolution of social groups that involves many steps: (a) individuals that happen to be in spatial proximity benefit simply by virtue of their number; (b) traits that are already present act as preadaptations and improve the efficiency of the group; and (c) new adaptations evolve under selection in the social context—that is, *via* interactions between individuals—and further strengthen group behaviour. The Dictyostelid or cellular slime mould amoebae (CSMs) become multicellular in an unusual way, by the aggregation of free-living cells. In nature the resulting group can be genetically homogeneous (clonal) or heterogeneous (polyclonal); in either case its development, which displays strong cooperation between cells (to the extent of so-called altruism) is not affected. This makes the CSMs exemplars for the study of social behaviour.

Introduction

Understanding the structure and functioning of cooperative groups from an evolutionary point of view requires that we pay heed to the role played by the social environment of an

individual. The social environment is determined by other individuals, which means that it can evolve along with the group. All members of the group constitute the social environment of any one of them, and a trait can be both the target of selection (when viewed in a member of the group) and its agent (when it influences the strength of selection on other members).

This leads to the concept of social selection, in which individual phenotype, and so individual fitness, is meaningful only in a given social context. Therefore the phenotype is ‘non-autonomous’: it depends on traits exhibited by other

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Insight, innovation, integration

An analysis of cooperative behaviour in the cellular slime mould amoebae (CSMs) offers insights into the evolution of social groups (at one end) and multicellular development (at the other). In the CSMs one can verify experimentally that the phenotype of an amoeba depends both on its own genotype and on the phenotypes of other amoebae: every individual in a

group forms part of every other individual’s environment. Thus the notion of individual phenotype is meaningful only within a clearly defined social context. Rather than shared genes, appropriately interacting phenotypes are the essential requirement for group life. These insights may be useful for understanding abnormal development as well.

individuals, whether those traits are similar or dissimilar to the one being monitored in the focal individual.^{1,2} For non-autonomy to be meaningful, the individual phenotype must be flexible or plastic, *i.e.*, capable of being influenced by the environment. An extreme case of plasticity is when different individuals of the same genotype give rise to different phenotypes in the same environment. Individual and group behaviour in the cellular slime moulds (CSMs) illustrate these concepts nicely, and also provide useful insights into the evolutionary basis of social behaviour in groups, including multicellular embryos—generally.

We first lay the groundwork by explaining our use of ‘social selection’ and ‘superorganism’; ‘non-autonomy’, ‘niche construction’ and ‘phenotypic plasticity’, terms that are relevant in the context of social selection, are introduced next. They are linked as follows: natural selection can act on phenotypes that depend on interactions with other phenotypes and so cannot be considered in isolation (social selection); social selection can take place in tightly organised groups of the same species (superorganism); the ultimate superorganism is the multicellular embryo; differentiation during multicellular development depends on reciprocal phenotype-moulding interactions between different cell types (non autonomy, niche construction); and behind it all is the capacity of single genotypes to exhibit different phenotypes (phenotypic plasticity). This will turn out to be somewhat discursive but should help the reader to appreciate that significant concepts have not always been used consistently, but for a good reason: it can help not to push definitions too hard and to retain a certain degree of elasticity in usage.

The second part sketches a plausible route for the evolution of group-level traits that begins with a purely physical advantage of increased size. Preadaptations reinforce those advantages by bringing into play similar traits in all members of the group. Next, group effects are reinforced *via* social selection for newly evolved reciprocal interactions between group members leading to division of labour. The examples that we list in support under these heads are mostly drawn from the social insects (the Volvocales are another well-studied case, not discussed here).^{3,4} The third and longest part of the paper draws attention to the fact that observations made on the development (or, equivalently, social behaviour) of the Dictyostelid amoebae or cellular slime moulds (CSMs) support the evolutionary route just sketched. Traces of the steps listed above can be seen in present-day CSM species, and there is considerable evidence for the importance of reciprocal interactions between cells. We end the paper by raising the question whether the concept of social selection can be useful for the study of not only normal, but also pathological multicellular development.

Social selection

Even a cursory survey of the literature shows that ‘social selection’ has meant different things to different people. The concept, though not the term, originates from Darwin’s pointing out that behavioural interactions between individuals of the same sex or different sexes (male-male competition, female choice) could lead to selection and phenotypic

evolution. Chance and Russell discussed social selection (again without using the term) in the context of allaesthetic behaviour, meaning ‘properties of animals (structures, colours, postures, movements, vocalisations, *etc.*) which produce behavioural effects on other animals’.⁵ Wynne-Edwards⁶ used ‘social selection’ to stand for an extension of sexual selection in which competition could operate within groups for any resource, not necessarily males. In a later work he made the important point that social competition resulted ‘in selection, . . . not so much for particular genes as for good all-round genotypes’, which meant that social selection had ‘a strong tendency to preserve genetic variance in the population’ (and preserve, as the context makes clear, phenotypic variation).⁷

Crook⁸ distinguished between four kinds of social selection based on (a) inter-individual competition for resources essential for reproduction, (b) competition for mates, (c) competition for resources required in the course of parental care, and finally, (d) cooperation towards establishing a social unit that would benefit the offspring of the co-operators and possibly their kin. According to him ‘social selection’ could accommodate conventional individual-level selection with no direct interactions (except possibly with offspring), sexual selection in the sense of Darwin and selection based on shared interests, whether or not the interests were identical. West-Eberhard⁹ discussed all this and more in a classic analysis. She drew attention to three features of social selection that are relevant for us: non-heritable variation, that can be significant for the maintenance of group life; facultative (as opposed to genetic) ‘switches’, that can lead to alternative behaviours in a social group, and, mutually exclusive tasks performed by the members of a group, which can follow from the above. Wolf *et al.*¹⁰ extended the quantitative treatment of interacting phenotypes begun by Moore *et al.*¹ and used ‘social selection’ to mean ‘a process distinct from other forms of natural selection’ which is likely to occur ‘whenever individual fitness varies as a result of interactions with conspecifics’. For Nesse¹¹ social selection was a ‘subtype of natural selection in which choices made by other individuals influence [an individual’s] fitness and change gene frequencies’: selection was followed by evolution, implying that the phenotypes (*i.e.*, different behaviours) in question were associated with different genotypes.

A slight rewording of Nesse’s formulation provides what in our opinion is a broad and practical definition of social selection: it is a form of natural selection in which phenotypes of other individuals influence an individual’s fitness. *Ipso facto*, social selection operates in groups, because the character of a group is defined by the extent to which its members interact. The interactions can be direct, mediated *via* another member of the group, or *via* the physical or (other) biotic environment. In the absence of any influence of one individual on another, ‘group’ would be just another name for a collection of individuals who, for all practical purposes, lead a solitary existence.

So social selection acts within groups, involves phenotypic interactions and has consequences for fitness. ‘Fitness’ can apply to the individual *vis-à-vis* the rest of the group or to the group in relation to other groups. Other qualifications can be

Table 1 Examples of the means, not mutually exclusive, through which social selection can occur in variously constituted groups.

Is inter-individual social selection mediated <i>via</i>	Group consists of						
	Predator and prey	Potential mates	Parasite and host	Two species (symbiosis/mutualism)	Cellular slime moulds	Social insect colony	Metazoan embryo
interacting phenotypes?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
shared reproductive interests?	No	Yes	No	Yes	Possible, not necessary	Possible, not necessary	Yes
different phenotypes?	Yes	Yes	Yes	Yes	Possible	Possible	Possible
different genotypes?	Yes	Yes	Yes	Yes	Possible	Possible	No

made as applicable in specific situations. Our emphasis is on phenotypic interactions between individuals within groups, whether or not they are accompanied by a ‘convergence of interests among group members’.⁹ Table 1 outlines the circumstances in which social selection can operate and the nature of the relevant group. Except for brief allusions, the rest of this paper does not deal with sexual selection or interactions between members of different species, though both are important topics, the latter particularly so for behaviour and multicellular development.¹²

The superorganism

Darwin spent a considerable portion of *The Origin of Species* wrestling with the problem of how the neuter state might have evolved in social insect workers: because they did not reproduce, even if selection acted on them, there could be no direct consequences for evolution.¹³ He got around the difficulty by comparing the queen (with her mate(s)) and the neuters to the germ line and soma: ‘natural selection, by acting on the fertile parents, could form a species which should regularly produce neuters’. Weismann concurred that ‘the whole colony [of a social insect] behaves as a single animal; the state is selected, not the single individuals; and the various forms behave exactly like the parts of one individual in the course of ordinary selection’.¹⁴

Despite these precedents, Wheeler is frequently credited with being the first person explicitly to draw an analogy between a social insect (ant) colony and a multicellular organism.¹⁵ He too compared the various sterile castes to somatic cells and the reproductive caste(s) to germ cells and subsequently coined the word ‘super-organism’ for social insects generally, because their colonies were akin to ‘a living whole bent on preserving its moving equilibrium and its integrity’.¹⁶ Fisher echoed Weismann in emphasising the unitary structure of a social insect colony but pointed out that whenever the queen was heterozygous at a locus, genetic variation between workers could be expected, and that could result in within-colony polymorphism and selection.¹⁷ Emerson¹⁸ expanded on the notion of a ‘biological individual’ as ‘an organized biological unit relatively independent of other units’ and proposed that entities ranging from genes to cells to multicellular organisms to societies (including those of social insects) and interspecific groups should be thought of as individuals, each at its appropriate level of organisation.

In the sources quoted above there is no attempt to restrict ‘superorganism’ to the highly eusocial insects. It is only recently that Hölldobler and Wilson have attempted to categorise superorganisms into different grades: ‘The social

organizations, however, vary greatly among the social insect species, and we can recognize different evolutionary grades of superorganismic organization . . . A “primitive” (less derived) grade is represented by several ponerine species, where members of the colony have full reproductive potential and there is considerable interindividual reproductive competition within each colony. Highly advanced grades are represented . . . by the leafcutter ant genera *Atta* and *Acromyrmex* and the *Oecophylla* weaver ants, where the queen caste is the sole reproductive, and the hundreds of thousands of sterile workers occur as morphological subcastes.’ They continue (questionably) with ‘These societies exhibit the ultimate superorganism states, where interindividual conflict within the colony is minimal or nonexistent’.¹⁹ Colony-level selection as the defining element of what constitutes a superorganism is a relatively recent development and has saddled the concept with unnecessary controversy. For us, *superorganism* will simply mean a group of individual organisms or cells that resembles a multicellular organism—that is, functions like an integral social or biological unit (taken from <http://www.bugsinthenews.com/Definition%20of%20Superorganism.htm>), with the added proviso that reproductive division of labour may or may not exist.

Multicellular development and social selection

Typically, metazoan development begins with a fertilised egg, the zygote, and ends with the differentiation of germ cells and highly diverse somatic tissue; both are needed to ensure that the genes of the parents are successfully transmitted. On its way to becoming an adult, the zygote goes through a large number of mitotic divisions accompanied by complex morphogenetic movements and tissue-specific patterns of gene expression.²⁰ If we ignore some well-recognised exceptions (*e.g.* the vertebrate immune system and somatic mutations that are neutral or affect gene functions that are not essential for normal development), the cells comprising the adult have the same genotype—for all practical purposes the adult is a clone. Therefore the genetic interest of any cell coincides with that of the whole organism (this may not be true among germ cells: being meiotic products, they need not be genetically identical). Because multicellular development is viewed as the acme of social behaviour, it has been an implicit belief that clonality must be the sole reason behind the extreme division of labour seen in embryos. However, the argument is incorrect. Everything else being equal, shared genes should improve the probability that selection can favour a trait in one individual that appears to benefit another individual (‘kin selection’), more so when the sharing extends to all genes. But the crucial point is that for two units to exhibit concerted

cooperative behaviour, their phenotypes must *covary* in an appropriate fashion,^{10,21} which does not require shared genes. Selection between interacting phenotypes is an obvious outcome to be expected when the individuals differ genetically. However, such selection can also act in genetically homogeneous groups, though ‘we will...not see its operation in most modern contexts, because conflicts between units of selection are evident only when a chimera is formed’.²²

There is abundant evidence for phenotype-phenotype interactions and feedbacks in multicellular development. The clearest instances come from what developmental biologists call regulative development.²⁰ In a regulative embryo the removal of a part of the embryo—sometimes as much as one-half—results in the reorganisation of the remaining portion, which goes on to form a normally-proportioned whole. The most dramatic demonstration of this was by Driesch, who showed that a single amphibian blastomere at the two-cell stage, that normally gave rise to a left or right half-embryo, would develop into an entire embryo if the other blastomere was removed.²⁰ The capacity of tissues to regenerate, and of body parts to maintain their relative proportions (analogous to regulation), are further evidences for the existence of intercellular communication, competition and feedback.^{23–25} Thus the requirements for social selection to act are present in embryos.

Not surprisingly, multicellular organisation has been compared to a society. Schleiden said so much before Darwin (whose comparison was in the opposite direction), apparently without referring to social insects. In 1858 Virchow made Schleiden’s analogy explicit: ‘[Schleiden]... declared that each cell has an individual existence, and that the life of an organism comes from the way in which the cells work together’ and ‘Rudolph Virchow took Schleiden’s observation a step further. He declared that “the composition of the major organism, the so-called individual, must be likened to a kind of social arrangement or society, in which a number of separate existences are dependent upon one another, in such a way, however, that each element possesses its own peculiar activity and carries out its own task by its own powers” (both quotations from Bloom²⁶).

Levels of selection

We are compelled to confront the issue of the level at which natural selection acts when we think of social selection acting in groups—for example in multicellular social groups that can be called superorganisms. It might appear that the preceding discussion has conflated selection at two levels. Concepts such as coordination and efficiency seem to call for a group-level view of selection; on the other hand competition and dominance are traits that reflect phenotypic differences between individuals within a group. Intuitively, to think of embryos as cohesive social groups with a unitary individuality seems self-evident; with colonial organisms that are constituted by the coming together of single cells, both points of view appear valid; whereas with social groups that are built by multicellular organisms (*e.g.*, social insect colonies), it appears strange to ignore the distinct individuality of each organism.

At the same time, the deep similarities between multicellular organisms and social groups cannot be ignored. As mentioned, Emerson was one of the many who drew an analogy between division of labour in social insects and somatic cell differentiation in multicellular development, with reproductives being compared to the germ line.¹⁸ He extended the analogy by bringing in other features: regeneration, the restoration of missing components (regulation), interactions between units and dominance, all of which are seen in social insect groups and embryos. These points have been advanced repeatedly by Bonner, with metabolic coordination, integration by means of mutual communication and specialised reproduction as the common underlying themes.^{27,37,38}

These commonalities risk being obscured by the assertion that the embryo is a constitutive structure (a group of genetically identical cells) whereas a social organism is a facultative entity (a group of genetically more or less diverse individuals). The assertion is valid but irrelevant. Ever since Price’s²¹ demonstration that trait frequency change in evolution can be partitioned into changes based on within-group selection and between-group covariance, we have known that individual selection and group selection, involving kin or otherwise, can be treated under a common rubric. To be sure, Price’s formulation has no bearing on the utility of one or the other description. In studying a trait and the factors that impinge on it, there may be more to be gained by focussing on the individual than the group, or the other way round; it depends on the situation. Also, in certain circumstances, both views may need to be adopted simultaneously (consider the example of a stray lioness attempting to join an existing pride). The virtue of Price’s formulation is that it separates the two central players in the evolutionary origin and maintenance of the group, namely (direct or indirect) competition within groups and between groups. In any case, as said above certain traits in social groups stand out as having a ‘group’ character, however much one wishes to adopt an individual-level viewpoint. Group longevity, which affects the success of the group and its constituents, could be an example. Longevity depends in part on metabolic efficiency, which is a collective property of the networks of food and energy transfer in the group.²⁸

Phenotypic plasticity, niche construction and non-autonomy

It is a common observation that in a given natural environment, the majority of a species is made up of individuals whose adult phenotypes are, for all practical purposes, the same. (It is noteworthy that the best-known exceptions involve phenotypic traits that are directly concerned with reproduction: inter-sexual dimorphism and intra-sexual polymorphisms.) They constitute the ‘wild-type’, the systematist’s ideal holotype. However, as we know today, the wild-type hides within itself considerable genetic variation which is cryptic or masked (‘buffered’). Buffering is adaptive and takes place thanks to the manner in which the coordinated functioning of different genes—broadly speaking, the developmental process—has evolved. C. H. Waddington, who devoted considerable attention to cryptic genetic variation and its consequences, referred to the buffering of the possible phenotypic consequences of genetic variation as the *canalisation* of development.²⁹

The concept of canalisation is related to that of norm of reaction and bears on the phenomenon of niche construction. ‘Norm of reaction’ implies that depending on the environment, the same genotype can express different phenotypes.³⁰ The path taken by developmental canalisation depends on the environment; therefore, instead of ‘the’ phenotype of an individual one should say ‘the range of phenotypes found normally in an individual of the same genotype’.

Canalisation and the norm of reaction point to contrasting aspects of genetic flexibility. Canalisation shows that different genotypes can lead to the same phenotype in similar environments, whereas the norm of reaction shows phenotypic plasticity: the same genotype can lead to different phenotypes in different environments. Multicellular development displays both features. The first aspect of genetic flexibility is exhibited, as already discussed, by the masking of genetic differences between different ‘wild-type’ individuals. Cell-type differentiation provides a striking example of the second aspect. Here the different environments may be dependent on positions within the embryo (*e.g.*, inside-outside differences in the mammalian blastula), parental influences (*e.g.*, *via* the egg cytoplasm, a maternal product, or within the maternal body) or phenotypes of other cells; different temporal environments, meaning different developmental histories, may also play a role. Phenotypes can differ even in the absence of a proximate cause. The genotypes and environments may be the same, but the developmental histories of the individuals in question may have been different (as Novick and Weiner showed of *Escherichia coli* and the lac operon).³¹ Finally, stochastic effects—‘noise’—can determine which of two alternative states of gene expression is actually chosen, and therefore which phenotype is expressed.^{32,33}

Phenotypic plasticity can be manifested in yet another way and that is in the phenomenon known as niche construction. ‘Niche construction’ originally referred to the ability of organisms to modify their environment—to have a hand in constructing their own niche and so to influence how selection acts on them (beaver dams and earthworm burrows are examples often cited).³⁴ It is a pervasive feature of the life cycle of many organisms and has been discussed as a likely major force in evolution.³⁵ Gilbert and Epel point out that niche construction is a useful concept in a rather different situation, that of interacting phenotypes in multicellular development.¹² As they argue, niche construction is another name for the phenomenon of embryonic induction (they go on to point out that it also applies to inter-organism interactions of developmental importance).

Embryonic induction is said to take place when signalling between two sets of cells that are in contact, and have each attained the appropriate competences, leads to differentiation. If the interaction fails to take place when it should, the course of differentiation is altered. An example from Gilbert and Epel is the ‘complex dialogue’ of reciprocal interactions that takes place in mammalian development between the neural tissue of the presumptive retina and the ectoderm of the presumptive lens, leading each to differentiate into its final state. Developmental geneticists inferred the existence of intercellular interactions from the observation that many mutations showed cell non-autonomous effects: the aberrant phenotype was manifested in

a cell which was itself genetically wild-type.³⁶ In the sense used by us, niche construction in embryonic development leads to non-autonomous differentiation; the fact that it does so implies that the cellular genotype can exhibit a range of phenotypes. The language and the conclusion apply equally well to individual phenotypes in social groups.

The steps to group living and social integration

We proceed to sketch a possible evolutionary route to social integration that can eventually become so strong that individuals become ‘trapped into group life, and group living may become virtually “obligatory” for them’.⁹ Our approach follows Bonner in attempting to ‘extend the principles of development to include the development of the whole association.’³⁷ He states a number of important general principles while discussing the evolutionary basis of division of labour, whether in groups of cells within an organism or groups of organisms.^{38,86,98,104} They may be summarised as follows. One, the functioning of living organisms involves ‘respecting physical laws as well as biological processes’; two, ‘the main cause of the appearance of division of labour ... is natural selection for efficiency’; three, ‘some aspects of division of labour can be explained by properties of similar units that exist in a group’; four, division of labour can come about from ‘somatic, physiological differences’ among individuals of the same genotype (here Bonner is referring to dominance hierarchies); and five, division of labour can be explained ‘by ... sensitivity to the [physical] environment as well as to the activity of [conspecifics]’ (this in the context of worker ants). We expand on his argument.

The phenomenon of more than one potential or actual unit of reproduction functioning as part of a larger whole (that is composed of similar or dissimilar units) is common in biology. The unit can be a gene or DNA sequence, a chromosome, an intracellular organelle, a cell, a tissue (organ) or an entire organism—a microbe, plant or animal. In many cases the whole displays ‘emergent’ properties, that is, modes of functioning that are not seen, or sometimes not possible, in its constituent units. When that happens, one should attempt to account for the property in question (“X”) in terms of the properties that the units display when examined separately; and only when that seems not to work, to look for other explanations.

Thus one should begin by seeing whether X can be explained as a straightforward consequence of the fact that the group consists of more than one unit. Perhaps X resembles what chemists call a colligative property, namely one that depends merely on number—for example, the elevation in the boiling point of a solution as the concentration of the solute is increased (except that in biology, the nature of the ‘solute’ cannot be ignored). Simply by being part of a crowd, so to speak, an individual may gain advantages. For example, the probability of capture by a predator could decrease. Or, because a predator must consider the risk of hurting itself in a physical collision (as with bird or fish flocks), numbers could act as a deterrent. In both situations the extent of protection should go up with group size. In the process, the group may develop a spatial structure that derives from nothing more

than each member acting independently in trying to do the same thing (e.g., staying as far from the periphery as possible).³⁹

The well-known 'square root of n' rule—more precisely, the Central Limit Theorem of statistics⁴⁰—may be behind apparent group-level adaptations that are an automatic consequence of group size. For example, given some distribution in the efficiency with which an individual performs a task, the performance of the same task by a group of similar individuals is expected to become ever more reliable as their number increases. Therefore, if (for example) an estimate of the amount of forage to be gathered in the future is important for running a beehive efficiently, it helps to increase the number of foragers. It has been proposed that this principle may have been one of the factors behind the evolution of sociality in bees.^{42,43}

In an environment that varies over space and/or time, the appropriate measure of long-term fitness (of the individual or the group as the case may be) is the geometric mean, which depends on both the arithmetic mean and the variance—in fact it decreases with increasing variance,⁴⁴ the essence of the argument goes back all the way to Daniel Bernoulli.⁴¹ Thus, given that variance decreases with size as discussed above, the commonly observed tendency of size increase in evolution⁴ may be a consequence of selection for the increased reliability that is provided by a larger size. A different advantage provided by number may be traced to the fact the ratio of volume to surface, and therefore a measure of how successfully a system can be maintained in a stable condition in the face of the tendency to equilibrate with the environment, increases as a function of the size (meaning typical linear extent) of the system. This too could have been a factor behind the evolution of multicellularity.

When a 'colligative' explanation does not suffice, one looks for an explanation at a different level. Now, over and above the properties of the individual units, one takes into account the interactions that occur between them. Here it is useful to make a distinction between two situations. Interactions could be based on traits that already existed in the solitary state; or, a trait in question may have been absent in single cells but evolved subsequent to the evolution of group living. The first situation involves a preadaptation which may or may not have served an adaptive role previously; if it did not, one would call it an exaptation.¹¹ A preadaptation that is relevant to group living is when an individual's traits vary in a stage-specific manner over the life cycle. For example, in both primitive⁴⁵ and advanced⁴⁶ social insects there is the phenomenon of age-polyethism, defined as a 'statistical shift in the activities of workers over time'⁴⁷; rather than absolute age, what counts is the relative age within a cohort. And when, as is likely, a randomly assembled group happens to contain individuals of different ages, the outcome can be adaptive division of labour.⁴⁸ Another possibility can be envisaged when the development of the traits of interest depends on a small number of inputs, in the extreme case just one. Then the individuals in whom the inputs happened to differ (even by chance), would exhibit different traits.⁴⁹

Thus group living would have been reinforced whenever the stability or the efficiency of the group was enhanced by the

expression of traits that were already present. However, if the units that made up a group had been living by themselves earlier, and if the initial selective advantage of group life was slight, solitary living and group living would have co-existed. The outcome can be compared to the equilibrium that is reached in a reversible chemical reaction of the sort $A \leftrightarrow B$, except that in our case A stands for solitary existence and B for group existence. The equilibrium situation reflects the relative *a priori* probabilities of the two states (and not, as in a chemical reaction, the probabilities of transitions between them). The coexistence of A and B would be favoured by spatial or temporal fluctuations in environmental conditions, or by trade-offs between the advantages of group life (e.g., improved chances of survival) and its disadvantages (e.g., lowered rate of reproduction). Alternatively, A and B could represent evolutionarily stable phenotypic compositions (ESCs) of genotypes.⁵⁰

A decisive step in the evolution of social behaviour must have been taken when 'truly social' properties emerged, based on traits that did not pre-exist but originated *de novo*. It is evident that the traits in question must have involved interactions between individuals. They would depend on signals from one individual that influenced the behaviour of a second individual in a way that fed back on the signaller. If the interests of the two individuals overlap little, signalling is selected or not depending on its consequences for the signaller and recipient, assessed independently. However, if the interests overlap significantly (say because the traits complement each other), the situation would automatically lend itself to selection at the level of the group; signalling between potential mates is an example. As far as any member of the group is concerned, all other members form part of its environment and specify the constraints to which it has to adapt; each member of the group is simultaneously actor and responder. If an adaptive outcome does evolve, it will be identified as a specifically group-level trait that improves the reliable maintenance of social behaviour while benefiting the long-term reproductive interest of the individual. A well-studied example of reciprocal feedbacks in group behaviour is the allocation of workers to different behavioural castes in a eusocial insect colony in which the relative proportions of different castes are restored by the group after they have been altered experimentally.⁵¹ As far as we are aware, the necessary manipulations have not been carried out on primitively eusocial insects. Still, the observations provide striking evidence of interactions between phenotypes and feedbacks in social groups.

Assuming that what we have called truly social properties exist, how should we go about looking for them, keeping in mind the fact that what we see may be the result of many generations of evolutionary modification? A good strategy would be to compare homogeneous and heterogeneous groups where the components that make up the heterogeneous group exhibit clear differences in traits when they form groups by themselves. For the strategy to work, the differences should reflect stable properties of the members of either group. Ideally, this means something correlated with the genotype. Then, each homogeneous group will be genetically uniform and the heterogeneous group will be genetically mosaic. Under these circumstances, if the phenotype of a member of the

heterogeneous group is influenced by the presence of other individuals, the influence can easily be detected. In the case of the cellular slime mould (CSM) or Dictyostelid amoebae, manipulations of this sort are straightforward and a huge amount of experimental data is available. In the next section, after a brief introduction to the CSM life cycle, we draw attention to diverse findings that can be interpreted within the framework of social selection.

Social selection and the cellular slime moulds

1. The life cycle: aggregation-driven multicellularity as a facultative response to stress. The Dictyostelid or cellular slime moulds (CSMs) achieve multicellularity in an unusual manner, namely by aggregation (see the books by Raper, Kessin and Bonner^{52–54a,b} for subtleties and details). These amoebae are ubiquitous in the soil or on animal dung. As single cells, they feed on bacteria and yeasts (or on synthetic media in the laboratory), grow and divide by mitosis. After food runs out, either the amoeba dies or one of many defensive reactions ensue and enable it to withstand the stress of starvation. An amoeba can encyst itself or, along with other cells, mount a collective response. Amoebae that are spread over a wide area (typically ~ one to a few mm²; the dimension of an amoeba is ~ 10 µm) can attract each other, come together at common collection points and collapse into aggregations. They do so by moving up spatial gradients of a chemical attractant released by some, if not all, of the cells (chemotaxis; the numbers can vary enormously, with a normal range of ~ 10²–10⁶), ref. 55–57 and <http://www.dictybase.org/Bonner%20paper.pdf>. Having formed the equivalent of an embryo in this unusual fashion, two outcomes are possible. The aggregate can proceed to differentiate in the manner of any metazoan embryo and form a terminal ‘adult’ structure, known as a fruiting body—this is during the ‘standard’ life cycle that is studied in the laboratory. Or, when cells of opposite mating types are present, the aggregate can get converted into a giant cell known as the macrocyst, which is the intermediate phase in an alternative, sexual, life cycle. The process is intricate (*e.g.*, in addition to nuclear fusion and meiosis it includes cannibalism) and favoured by special circumstances (*e.g.*, flooding by water).⁵⁸ CSM species, and even different genotypes within the same species, differ in their propensities to form microcysts, macrocysts and fruiting bodies; and more than one structure can be seen in the same culture plate. It would be of the utmost interest to know the relative probabilities of these developmental strategies under various conditions; the point of interest is that there is a great deal of developmental flexibility in the response to starvation. From now on, we will deal mostly with the life cycle that involves the fruiting body.

Post-aggregation development involves a constant number of cells (in the laboratory, after one has taken into account stragglers in the cell division cycle that may divide soon after the food supply is removed). Aggregation is followed by complex morphogenetic movements both within the mass and by the mass as a whole, giving rise finally to a terminally differentiated ‘adult’ structure known as the fruiting body. Within the fruiting body, some cells make up a ball of

stress-resistant spores and other cells form a stalk of dead cells that supports the spore mass at its end. This arrangement, with spores raised above the substrate, is believed to aid passive dispersal. If dispersal occurs to an environment where food is available, each spore can germinate and the amoeba that emerges can feed, grow, divide and set off a new multicellular stage after the food runs out.

Spores can be compared to germ cells and the stalk can be thought of as the equivalent of somatic tissue. However, in contrast to the cells of a metazoan embryo, the CSM amoebae that form a social group need not be genetically identical. Under natural conditions they can constitute a clone,⁵⁹ belong to different genotypes within the same species,^{60–64} or, rarely, belong to different species, ref. 65 and unpublished work. When an aggregate is genetically heterogeneous, phenotypic heterogeneity can be a reflection of diverging reproductive interests between the amoebae in a group. Even if the aggregate consists of a clone of cells, individual reproductive interests need not coincide: phenotypic differences between cells can be expected to be translated into reproductive differences (as indeed they are). Here, though the situation appears to lend itself to a kin-selection based explanation, one must keep in mind that what may be at work is individual-level selection and physiological dominance.⁶⁶ The presence of different genotypes in a group makes the likelihood of phenotypic differences more likely, and also easier to verify.

CSM development occurs within a specified range of the physical environment, and its outcome can differ significantly within that range. In *Dictyostelium discoideum*, a decrease in humidity speeds up development,⁶⁷ whereas a decrease in temperature slows it down⁶⁷ and increases the distance over which amoebae can be attracted.⁶⁸ Starved cultures develop faster, and aggregates are smaller, in light than in the dark.⁶⁷ These effects of light are marked in the case of *Polysphondylium pallidum*, in which aggregation cannot commence in the dark.⁶⁹ The nature of the substrate on which development occurs also has a significant effect on development (for example, whether it is relatively smooth or granular), ref. 70 and unpublished work.

Interestingly, there can be significant differences between supposedly wild-type strains in the biochemical details of development. A prominent instance involves variations in the kinetics of production and release of two proteins that modulate the strength of the cAMP signal between its release by one *D. discoideum* cell and reception by another, namely a secreted cAMP phosphodiesterase and its inhibitor.^{71,72} The implication is that the norm of reaction for the species as a whole—with its members being of different ‘wild-type’ genotypes—extends over a broader range than the norm for a single individual. Not unexpectedly, mutants show a stronger sensitivity to environmental conditions than the wild-type does, which points to a component of Genotype × Environment interaction in overall phenotypic variation. For example, some mutants of *D. discoideum* are unable to aggregate on growth medium—that is, when they are plated with bacteria on glucose-peptone agar—but develop normally when plated without food on deionised agar.^{73,74}

2. Advantages to group living as a fall-out of increased size.

Spatial clustering, which was conceivably the precursor to aggregation by chemotaxis, can arise simply as a consequence of large numbers. This was shown in a simulation by Houchmandzadeh⁷⁵ who found that within a certain range of the relevant parameters, a combination of events involving the birth, uncorrelated random dispersal and death could lead to strong clustering. The result was confirmed by observations on clonal growth of *D. discoideum* amoebae on a surface.⁷⁶ The speed of migration of CSM aggregates (slugs) increases with their size (or more accurately, length).^{77,78} The implication is that the larger the number of amoebae in a group, the better the chances for any cell to disperse to a more favourable environment. Size can favour dispersal in another way, which is by raising the spore mass to a greater height above the soil. Kessin *et al.* showed that differentiation into spores permitted amoebae of *D. discoideum* to survive after being eaten by a soil nematode.⁷⁹ It may be that aggregation *per se*, via an increase in size, also acts as a defence against nematode attack. Nanjundiah and Bhogle⁸⁰ found that the reliability of differentiation, measured as the variance in spore or stalk cell proportion relative to the mean, decreased as the size of the aggregate increased, though only a part of the decrease could be attributed to cell number *per se*.

3. Phenotypic differences among individuals of the same genotype; division of labour

(a) *Spontaneous or 'random' variation.* Cell to cell differences in behaviour can be observed in clonal populations of *D. discoideum* right from the onset of starvation. Starved cells develop a number of competencies in the course of aggregation. One, they synthesise and release the chemoattractant, cyclic AMP, in a pulsatile fashion;⁸¹ two, they sense, amplify and relay an external cAMP stimulus;^{82,83} three, they sense and respond to an external source of cAMP by moving towards it;⁸⁴ and four, they develop an intercellular cell adhesion system.⁸⁵ These competencies arise in all cells roughly in reverse order, albeit with some overlap and not synchronously.^{86,87} Their appearance can be speeded up and reinforced by providing external pulses of cAMP.^{87–89} The onset of competence (d) is at about the same time or somewhat after (b). Superficially, the situation appears to be different in *P. violaceum*, where a case can be made for a specialised 'founder cell' becoming the centre of an aggregate. But here too, if a founder is removed, another cell replaces it, though after an appreciable amount of time;⁵⁷ the essential difference between the two species seems to be one of heterochrony.⁹⁰ Early variation may not be without consequence: in *D. discoideum* a positive correlation has been found between the probabilities of a cell initiating aggregation and ending up as a spore.⁹¹ The simplest explanation of the visible heterogeneities that accompany early aggregation—some cells at the centre of aggregation, ramifying streams and single cells moving towards a stream or directly towards the centre—is that they are due to random physiological differences between cell and cell reflected as cell-to-cell variations in the onset of developmental competences.

(b) *Factors that accentuate spontaneous variation.* In *D. discoideum*, at the time that they begin aggregation, the

amoebae already have stalk-forming or spore-forming tendencies; the evidence is mostly indirect. When a suitable external bias is imposed, of a type that can exist under natural conditions (for example differences with respect to the energy content of the food;^{92,93} or variations in time of starvation relative to the phase of the cell division cycle,^{94,95} the bias makes it more or less likely that an amoeba differentiates into a spore).^{66,95–99} Even in the absence of any external bias, spontaneously occurring cell-to-cell variations in cellular calcium enable a correlation to be made between 'low calcium' and spore-forming tendency and 'high calcium' and stalk-forming tendency.¹⁰⁰ Interestingly, 'high' and 'low' refer to relative, not absolute differences. Data on other species are meagre, but it is known that some of them (*e.g.*, *Polysphondylium* species) do not show a clear distinction between presumptive stalk and spore cells. *D. mucoroides* makes prespore cells, of which some get converted to stalk cells as the slug migrates.^{101a} In *Acytostelium leptosomum*, the stalk is an extracellular structure made by all (presumptive spore) cells.^{101b} Therefore the question of different cell types does not arise—unless, as may be the case in *D. discoideum*,^{98,102} spores can exhibit functional differences.

(c) *Interactions between cells belonging to different phenotypes.* Right from the onset of aggregation, interactions between cells are central to the entire process of development. However, the features of development discussed above in (a) and (b) can be accounted for either as outcomes of stochastic processes or as arising from inter-individual variations based on differences in pre-aggregation environments. Now we take up examples of interactions based on phenotypic differences that have already built up. They show the role of intercellular interactions most clearly; their outcome is that the phenotype of one cell depends on that of another.

The single most striking piece of evidence in favour of intercellular interactions is that the ratio of differentiated cell types is approximately invariant with respect to total cell number over two to three orders of magnitude—what has been called 'the supreme problem of differentiation' in the cellular slime moulds.^{54a} More to the point, the relative proportions of stalk to spore cells can re-adjust if the developing mass is fragmented, even if most cells in the fragment belong to a single (presumptive) cell type¹⁰³ (again pointing to relative differences in phenotype rather than absolute phenotype as the essential element that leads to functional differences). The actual proportions of the two differentiated cell types range from about 20:80 in *D. discoideum* to 50:50 in *D. giganteum* (for wild type strains studied under standard laboratory conditions).^{67,104,105}

It turns out that in order to account for the magnitude of the fluctuations in cell type proportions (mentioned earlier), one has to invoke, over and above a purely stochastic basis for cell type determination, reciprocal negative feedbacks between the presumptive cell types and an ability on the part of a cell to sense the number of cells in its social group.⁸⁰

Group integrity within the aggregate is maintained by intercellular adhesion and cell-to-cell signalling. Though all cells take part in these, there are significant differences between the two presumptive cell types in traits related to adhesion and

cAMP signalling.¹⁰⁶ The bulk of the motive force for the movement of the slug is provided by cells in its front.¹⁰⁷ Besides constituting a minority (~20%) of the total number of cells, these anterior cells die as they become part of the stalk. In an interesting partial overlap with *Acytostelium*, where the stalk is wholly extracellular, *Dictyostelium* cells first secrete an extracellular stalk tube, then form the stalk proper by moving into the tube, dying, and synthesising a cellulose wall.⁵³ Eventually the slug stops moving and begins to erect itself while terminal cell differentiation into stalk and spore is taking place. Spore differentiation requires that presumptive stalk cells signal by means of a small peptide SDF-2.^{108,109} The cells that will eventually sporulate climb up the stalk, and their ascent is helped by two ‘cups’ of cells that cradle the presumptive spore mass from above and below. Of these, the lower cup appears to provide mechanical support while the upper cup actively lifts up the presumptive spore mass.^{110–111} Neither lower cup cells nor upper cup cells sporulate; they are believed to die while remaining amoeboid in morphology.¹¹²

4. Intercellular interactions and phenotypic heterogeneity accompanied by genetic heterogeneity. Because of the manner in which the CSMs become multicellular (*i.e.*, by aggregation of spatially separated amoebae), it is possible that the amoebae that come together belong to different genotypes. In accordance with this expectation, fruiting bodies formed under natural conditions (or under laboratory conditions that may mimic what happens in nature) can be genetic chimeras.^{63,64} The presence of multiple genotypes in the same aggregate or same fruiting body carries with it implications for the evolution and maintenance of social behaviour in the CSMs, because the stable coexistence of different genotypes requires that stringent conditions be fulfilled.¹¹³ For example, everything else being equal, if an amoeba has a lower probability of sporulation than one belonging to another genotype, the frequency of its own genotype should fall steadily from one generation to the next. Genetic heterogeneity within groups is easily achieved by mixing cells belonging to two or more clones, and most of what we have learnt about behaviour in mixed genotype groups comes from laboratory experiments. As will be seen, the consequences of mixing experiments are extraordinarily diverse. But they carry a common lesson: phenotypic plasticity is a pervasive feature of the division of labour displayed by CSM social groups. The phenotype of a cell, and therefore of the group, is strongly influenced by intercellular interactions. This makes it plausible that plasticity, or developmental flexibility, must have been central to the evolution of sociality in the CSMs.

(a) *Synergism between naturally occurring strains that differ in their developmental phenotypes.* Starting from the spores in a natural isolate of *Dictyostelium mucoroides*, Filosa managed to obtain four clones of amoebae that, when observed separately, displayed distinct behaviours: one developed normally and the remaining three gave rise to aberrant-looking fruiting bodies.¹¹⁴ One of the aberrant forms, MV, formed spores at a low efficiency and did not form a wild-type stalk. A wild-type + MV mix developed like the wild-type and, after many cycles of growth and development, attained a stable

equilibrium in which the relative proportions were ~90% wild-type: 10% MV.

Buss obtained two *D. mucoroides* strains in close proximity in the soil.⁶⁰ When studied in isolation, both displayed stable but distinct phenotypes: one went through normal development whereas the other did not. After starved amoebae of the second strain aggregated, all of them differentiated into spores that remained on the surface; the aggregate did not form a stalk. The indications are that the strains were genetically distinct, though they may have been related (there is no evidence bearing on the issue). When mixed, as must have been happening in nature, the two strains developed in concert and formed chimaeric fruiting bodies. However, the two components differentiated in a way that depended on the composition of the mix. When the ratio of ‘stalkless’ to normal amoebae was very low, ‘stalkless’ amoebae were over-represented in the spore population; and when the ratio was very high, the ‘stalkless’ strain formed fewer spores than expected. In other words, there was a frequency dependence of just the sort required for a stable equilibrium to be attained—as turned out to be the case. Thus, everything else being equal, the two would be expected to co-exist stably in nature. In this case, the nature of the interaction is such that it serves little purpose to use words such as parasite, cheater or altruist as descriptors of the phenotype of either strain. Depending on the circumstances, any of these labels can be attached to any of them; it is the dynamics of their interaction that is relevant.

Kawakami and Hagiwara found that *P. pallidum* strains that belonged to complementary mating types also differed in aspects, including fruiting body morphology, in their asexual life cycles,¹¹⁵ indicating a more usual type of ‘synergism’—mutually beneficial interactions between a pair of individuals belonging to different phenotypes. Moreover, it is an unusual example of genotypes switching roles, by giving rise to sexual dimorphism (in one context) and cooperating within a social group (in another context). This is reminiscent of a school of fish in which an individual of one sex changes into another sex in response to a change in the social structure of the population—for example, when the dominant position falls vacant, except that role-switching in fish is a form of temporal polyethism (for an evolutionary perspective on sequentially hermaphroditic fish, see ref. 116). A curious example of what could be cross-species synergism between a CSM and a fungus was found by Ellison and Buss (though only a benefit to the CSM was established).¹¹⁷ They isolated normal looking fruiting bodies of *D. mucoroides* along with the fungus *Mucor hiemalis* from soil samples. After purifying the two separately, they noted that when allowed to develop by themselves, the amoebae of *D. mucoroides* aggregated and differentiated straightaway into a ball of spores; intermediate developmental stages were absent. However, when their environment included fungal hyphae, or if they were provided access to a diffusible substance released by the fungus, the amoebae went through normal development.

(b) *Synergism between wild-type and mutant phenotypes.* Sussman and co-workers isolated many spontaneously occurring and artificially generated (*e.g.* after UV treatment) developmental

mutants of *D. discoideum*. Among them, some were unable to complete development whereas others went through development and produced abnormal-looking fruiting bodies.^{73,118,119} Either a mixture of cells derived from two mutant strains or a wild-type-mutant combination was studied to see whether the presence of one genotype influenced the other. In many cases the outcome was normal development. For example: a combination of the wild-type and an aggregateless (agg^-) mutant, when plated at a low density at which the wild-type was unable to aggregate (below 100 amoebae mm^{-2}), formed normal aggregations, and it appeared that the presence of the wild-type induced the agg^- cells, not just to participate as responders to the wild-type, but also to form aggregation centres too. However none of the spores isolated from chimaeric fruiting bodies formed by agg^- and wild-type amoebae were of the agg^- type.¹²⁰ Similarly, many pairs of developmentally aberrant mutants were able to complement each other's defects when mixed and go through normal development.^{73,118,120,121}

Similar experiments were carried out by Weber and Raper,⁷⁴ who found that two agg^- mutants of *D. discoideum* aggregated and formed normal fruiting bodies when they were put into contact with wild-type *D. discoideum* amoebae or even amoebae of other species such as *D. purpureum* and *D. mucoroides*. A plausible explanation of the outcome comes from the observations of Darmon *et al.* that the developmental defect in many agg^- mutants of *D. discoideum* could be cured by periodic stimulation of starved cells with extracellular cAMP.⁸⁸ Ennis *et al.* isolated a *D. discoideum* mutant that exhibited aberrant developmental morphology and poor differentiation.¹²² When mixed with its parental wild-type strain, the mutant participated in normal development and was more efficient than the wild-type at forming spores: its proportions kept increasing with each developmental cycle. Huang *et al.* showed that a very small proportion of wild-type cells (probably a single cell) was sufficient to initiate development in an otherwise agg^- mutant.⁹¹ Clark found a low incidence of synergism when pairs of developmentally defective mutants of *Polysphondylium violaceum* were mixed.¹²³ On the other hand, Rafaeli found that the wild-type and mutant or two different mutants (for example, *Stumpy* and *Fruity*) formed chimaeric, normal fruiting bodies.¹²⁴

Sussman¹²⁰ and Kahn¹²⁵ made an extraordinary observation pertaining to synergism in their experiments with *D. discoideum* and *D. purpureum* respectively. They reported that a single round of joint development between an agg^- mutant and the wild-type (in the course of which mutant cells participated in normal development and differentiated into stalk and spore cells) was sufficient to transform the mutant's phenotype. Thereafter, mutant cells were competent to aggregate and differentiate by themselves. A parallel finding was made by Kaushik.¹²⁶ She mixed spores of three strains of *D. giganteum* (46a3gig, 46d2gig and 46c6gig) in pairs as well as in three-way mixtures and grew them in the presence of bacteria for approximately 24 generations. After that, spores from the resulting fruiting bodies were spread with bacteria on nutrient agar plates at a very low density. When they germinated they cleared the bacterial lawn around them forming plaques. Interestingly, many of the plaques when transferred to other

plates and allowed to grow and develop further, could not do so. Some of the plaques did not proceed beyond loose aggregations and a few of them did not aggregate at all.

(c) *Antagonistic interactions.* Examples are known in which cells of the same CSM strain affect each other negatively. Amoebae of *D. discoideum* repel each other during growth, as do *D. purpureum* amoebae. *P. violaceum* amoebae do not repel each other but move away from a diffusible product released by *D. discoideum*,¹²⁷ which could affect the distribution of the two species in areas of co-occurrence. During the normal post-aggregation development of *D. discoideum*, presumptive spore and stalk cells—which at an early stage of development are better termed 'high quality' and 'low quality' amoebae respectively⁶⁶—interact in a remarkable manner that points to phenotype-dependent developmental plasticity as the basis of division of labour. *D. discoideum* cells synthesise and release a family of variously modified membrane-permeable chlorinated phenolic compounds that are lethal and are generically known as DIF, meaning 'differentiation-inducing factor'. The name derives from their ability to induce amoebae to die and differentiate to a stalk cell-like condition. DIF-1 is the most potent of them. As predicted⁶⁶ and subsequently verified,^{128,129} DIF-1 is made predominantly by high-quality amoebae at the back of the slug. Not only that, it is broken down by low-quality amoebae in the front of the slug¹²⁹; this happens even when the amoebae belong to the same clone.^{66,128–130}

There are also cases from mixed genotype cultures where cells of one genotype repress the development of the other. 50d8, a wild-type strain of *D. giganteum*, aggregates and forms normal fruiting bodies when by itself, but does so only rarely when mixed with amoebae of the (also wild-type) strains 46a3, 46d2 or 46c6. The inhibitory effect appears to depend on cell-cell contact, because 50d8 develops normally when separated from any of the others by a filter paper barrier.¹⁰⁴

Mujumdar *et al.* (unpublished work) found that when a minority of *trishanku* mutant cells are mixed with wild-type *D. discoideum*, aggregation streams break up and fruiting bodies are smaller than normal—phenotypes characteristic of the mutant.¹³¹

The antagonism between strains can be mediated *via* bacteria, which are their normal food. Following growth and starvation, amoebae of the *D. discoideum* mutant *Agg*⁻208 aggregated on a 'minimal agar' medium that had been repeatedly washed with distilled water, but did not do so even after the food was exhausted if they were allowed to remain on growth plates; another mutant, *Agg*⁻206, did not aggregate under either condition. Co-development of these two mutants on minimal agar led to the partial or complete loss of *Agg*⁻208's ability to aggregate.⁷³ Weber and Raper found that two developmentally aberrant mutants of *D. discoideum*, *agg*⁻1 and *agg*⁻2, aggregated on non-nutrient agar but when grown on plates containing *Escherichia coli*, did not do so even after food depletion.⁷⁴

(d) *Complex interactions between wild-type strains.* Experiments with *D. mucoroides*,⁶⁰ *D. discoideum*^{64,132} and *D. giganteum*¹⁰⁴ have shown that in mixtures of different strains of a species, the efficiency with one of the members

of a pair sporulates (meaning the ratio of the number of spores formed to the starting number of amoebae) is different from its sporulation efficiency when by itself. In some of these cases, both strains were wild-type and in other cases one or the other member of the pair was a mutant. After a number of different strains are mixed pair wise, it turns out that the strains can be arranged in a linear transitive hierarchy of relative sporulation efficiencies, akin to a pecking order or dominance hierarchy.^{104,133} In the case of *D. giganteum*, the presence of a third strain in the mixture shows that the underlying interactions are in fact non-linear—the strain that is predicted to be lowest in the hierarchy can do as well as the other two.¹⁰⁴ In *D. discoideum* too, it turns out that the quantitative outcome pertaining to relative sporulation efficiency in pair wise mixes is not predictable from the outcome of mixing the same strains separately with a third strain. Khare *et al.* worked with three stains, wild-type, *chtC* ('cheater') and *recA* ('cheater resister').¹³⁴ In wild type + *recA* or *recA* + *chtC* mixtures, the contributions of the two components to the spore population are approximately the same; but in a 1:1 wild type + *chtC* mixture, *chtC* forms more spores than the wild type. However, in a three-way mixture *chtC* forms fewer spores than expected. Finally, a loss of function mutation in *hdaB*, one of the four genes known to code for histone deacetylase, does not lead to any obvious change in the development of *D. discoideum*. However, when mixed with the wild-type in a 1:1 ratio, mutant cells form fewer spores than the wild type.¹³⁵ Santorelli *et al.* have reported a complementary case, in which a *D. discoideum* mutant forms more spores than the wild-type when mixed with it in a 1:1 ratio, but develops normally when by itself.¹³⁶

Discussion

Thanks to the unusual route adopted by them to achieve multicellularity, the CSMs display traces of all the steps that can plausibly be envisaged as having taken place in the transition from unicellular life to full-blown group behaviour, whether in groups of cells (as in embryos), or in groups of metazoan individuals. Still, the CSMs that we study today must have an ancient evolutionary history. Therefore, in a strict sense, today we can expect to identify only the factors that lie behind the maintenance of traits, not the factors that were responsible for their origin. However, one can argue on grounds of plausibility that there is likely to be an overlap between the factors that led to a trait evolving in the first place and the factors that are responsible for its maintenance. Precisely because of the nature of the CSM life cycle, we can perceive traces of those steps more clearly than we might hope to in organisms that achieve multicellularity *via* continued divisions of a zygote. In this respect, the CSMs offer advantages for studying the evolution of social behaviour similar to those provided by primitively eusocial insects.¹³⁷ One might say that they too are 'superorganisms' in which many individuals live in stable groups with division of labour. There are other organisms in which spatially separated multicellular units form by aggregation, including myxobacteria,¹³⁸ myxomycetes¹³⁹ and the ciliate *Sorogena stoianovitchae*,¹⁴⁰ but in hardly any of them do we have experimental evidence in

comparable detail to that in the case of the cellular slime moulds—including knowledge of whether aggregations can be genetically heterogeneous (as in the CSMs) or not. In the colonial ascidian *Botryllus schlosseri*, individuals can fuse and give rise to chimaeras containing more than one genotype. Rinkevich and Shapira found that chimaeras made up of four genotypes had advantages over ones that contained two or three genotypes—they grew more rapidly and survived longer¹⁴¹ (a complication in interpreting their findings is that group size may have influenced the outcome; it went up with the number of clones).

Equally, because they often exist in multi-clonal groups, the CSMs are a useful guide to understanding multicellular development from an evolutionary point of view. On the face of it this appears unlikely—it tends to be taken for granted that all features of development in a clonal embryo can be explained on the basis that what is 'good for the whole' is *ipso facto* 'good' for any cell. But there are many reasons for saying that the study of development in a polyclonal group is meaningful for understanding cell behaviour in clonal groups. To begin with, if our interest is in the evolution of group behaviour, what matters is that the group is made up of individuals with different phenotypes and therefore intrinsically different capacities to reproduce (as members of the group); and different phenotypes are just as likely in genetically homogeneous groups as within heterogeneous groups. Second, it has been argued that the reason why only some cells differentiate into germ cells is because by virtue of their phenotypes they out-compete the others and, in a sense, compel them to contribute to somatic tissue,^{60,142} a line of argument that has also been used to explain the evolution of differentiation in the CSMs.⁶⁶ Third, the inevitability of somatic mutations implies that so-called clonal development actually involves groups whose members may not be genetically identical.¹⁴³ Thus CSM development, and by extension that of intra- and inter-specific chimaeric embryos,^{144,145} may have much to tell us about the evolution of development in general. The life cycle of Dictyostelid amoebae has long been viewed as an example of multicellular development that throws up interesting questions when viewed from an evolutionary perspective. It is time to turn tables and, as integrative biologists, ask what new insights into normal and abnormal development we can gain by thinking about the evolution of cooperative behaviour in the cellular slime moulds. The same point applies with regard to social behaviour in larger animals. The fact that a starved amoeba can differentiate into a spore or stalk cell depending on the phenotypes of other amoebae implies plasticity of a high order. This is mirrored in the functional plasticity displayed by primitively eusocial or facultatively social insects. Workers can take over a queen role when the opportunity presents itself;¹⁴⁶ distinct behavioural biases that impinge on social roles can be found in largely solitary species¹⁴⁷ and the biases can be overridden by social competition.¹⁴⁸

On the basis of studying the evidence for socially selected traits in CSM groups, two broad generalisations may be made. The first is that whenever social selection operates on a phenotype, it is impossible to draw a distinction between 'cell-autonomous' and 'cell-non-autonomous' effects of the

underlying genes. The second is that it is inappropriate to label genotypes by words such as ‘selfish’, ‘altruist’, ‘cheater’ and so on (‘noble’ has joined the list recently). That is because at best such words can convey a verbal description of traits expressed in very specific, and therefore restricted, social settings. In general, they convey nothing about how cells of the same genotype might behave in groups containing some other set of genotypes. Both comments are in the same spirit as that pertaining to the phenotype of a single individual. Namely, it is inappropriate to associate a phenotype with a gene (or allele). Rather, the phenotype results from a complex interplay between allelic activity and the rest of the genome, that too in a specified environment. When every individual is part of every other individual’s environment, the phenotype of any one depends on the phenotypes of the rest. In a literal sense, the phenotype of the individual is a social construct.

Moore *et al.*¹ and Frank² have discussed the principles of social selection with the help of a general method for partitioning phenotypic variance that, as mentioned earlier, was pioneered by Price.²¹ The method awaits application to genetically heterogeneous groups, especially when their behaviour is pathological. Evidence is accumulating that many cancers can be described as the consequences of social networks that malfunction.¹⁴⁹ Among the attendant factors are phenotypic heterogeneities between the members of a cellular group and, just as in ordinary development, reciprocal interactions between cells and their cellular and extracellular environments (*i.e.*, cellular non-autonomy).^{150–152} But the outcome is to derail the normally stable structure of the group. An analogy has been made recently between groups of cancer cells and species.¹⁵³ It would be worthwhile to examine whether pathological development, including of the sort that leads to cancer, can be analysed usefully within the Price framework as an example of social selection that has gone awry.

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