

Evolutionary transitions in individuality: insights from transposable elements

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The history of life has been characterised by evolutionary transitions in individuality, the grouping together of independently replicating units into new larger wholes: genes to chromosomes, chromosomes in genomes, up to three genomes in cells, and cells in multicellular organisms that form groups and societies. Central to understanding these transitions is to determine what prevents selfish behaviour at lower levels from disrupting the functionality of higher levels. Here, I review work on transposable elements, a common source of disruption at the genome level, in light of the evolutionary transitions framework, and argue that the rapid influx of data on transposons from whole-genome sequencing has created a rich data source to incorporate into the study of evolutionary transitions in individuality.

Conflict and cooperation across the hierarchy of life

Although the study of social evolution (see [Glossary](#)) has long focussed on the baboon troop, the beehive, and, more recently, that of social microbes, most cooperation occurs within organisms [1–4]. Genes come together in chromosomes, which comprise genomes, and several genomes coordinate efforts in the cells that comprise multicellular organisms, which in turn often form tightly knitted social groups [2,3,5,6]. The coming together of previously independently reproducing units into new larger wholes is what gives life its hierarchical organisation [2,5,7–9]. Inspired by the research programme on major transitions in evolution, the points at which one level of the hierarchy becomes subsumed into another have become known as evolutionary transitions in individuality ([Box 1](#); [Table 1](#)). The functionality of a given level in the hierarchy is contingent on the suppression of conflict at lower levels [3,5,7,10–12]. Therefore, under this view of life, the problem of evolution is to understand the mechanisms that make cooperation thrive over conflict at a given level.

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Each transition in individuality can be divided into three stages ([Figure 1](#) [3]). First, social group formation is the origin and spread of social behaviour in a population. Second, social group maintenance concerns the processes that enable the social group to persist in a stable way. Third, social group transformation is the origin of a new level of individuality. The origin of the genome from independently replicating molecules was not only the first transition, but the genome can also be said to be the most fundamental level of cooperation. Whereas many organisms thrive without the benefits of multicellularity or eusociality, cooperation among genes occurs in all organisms.

The idea that the same principles of social evolution theory can be applied to all transitions in individuality has been around for some time [2,3,5,13,14]. However, given that most of these transitions occurred in the distant past, empirical work has often been limited to the later transitions. The origin and maintenance of cooperation among individual organisms has perhaps received the most attention. Pioneering workers in the field concerned themselves primarily with the social lives of animals [15]. Over the past few years, many researchers have fruitfully applied

Glossary

Hypercycle: a network for self-replicating units, where the product of a given reaction acts as a catalyst for the next in a cyclical manner. For example, in the hypercycle of members A, B, and C, A catalyses B, B catalyses C, and C catalyses A.

Genomic conflict: conflict in the fitness interests between genes in the same genome.

Linkage disequilibrium: the nonrandom association of alleles at two or more loci.

Modifier: a gene that evolved to oppose the effect of a selfish genetic element.

Selfish genetic element: genes that have the ability to promote their own transmission at the expense of other (unlinked) genes in the same individual.

Silencing: the interference with the expression of transposable elements, often resulting in a reduction of the transposition rate to zero. Silencing is often administered by siRNAs.

Small interfering RNAs (siRNAs): short (20–25 bp) double-stranded RNA molecules that interfere with the expression of certain genes with complementary nucleotide sequence. siRNAs have an important role in the silencing of transposable elements.

Social evolution: the study of the evolution of social behaviour. Traditionally restricted to animal societies, but its expanded version deals with all levels in the hierarchy of life.

Transposable element: stretches of DNA that can move to new locations in the genome, either through a ‘copy-and-paste’ mechanism via an RNA intermediate (Class 1 retrotransposons) or via a cut-and-paste mechanism (Class 2 DNA transposons).

Box 1. Major transitions in evolution and individuality

Not all major transitions in evolution are evolutionary transitions in individuality. In their landmark publication, Maynard Smith and Szathmáry [5] presented eight major transitions (Table 1, main text). In their opinion, what these events had in common was that they changed how the evolutionary process itself operates. More specifically, most of them share three features. First, following the transitions, units that previously reproduced independently can now only reproduce as part of a larger whole. Second, a division of labour characterises the new units. Third, the transitions change the language of information and the way in which information is stored and transmitted. However, these features do not apply to all transitions. For example, the evolution of the genetic code is a good example of division of labour and a change in the language, storage, and transmission of information, but does not involve the coming together of previously independently reproducing entities. For it to be useful to study transitions as a group, there is a need for conceptual unity [2,87]. Without conceptual unity, they may as well be grouped together under the heading 'a list of interesting and important events in the history of life'.

Focusing on transitions in individuality offers one route to such unity. Evolutionary transitions in individuality share two main themes [2,3]. To start, just like the first feature identified by Maynard Smith and Szathmáry, transitions involve the emergence of cooperation among independent units leading to the formation of a new higher-level unit. Second, crucial to the functioning of this new unit, the transitions are associated with the evolution of mechanisms to suppress conflict among lower-level units. This approach typically removes the genetic code, sex, and language from the list of transitions, but one may add interspecific mutualisms to the list.

the same approaches to the study of interspecific mutualisms [16] and recent transitions from uni- to multicellularity [17]. Pioneering theoretical work on the transition from genes to genomes was done by Eigen and Schuster through their work on the theory of hypercycles [18–20] to explain the origin of networks of interacting genes. This approach was later thoroughly extended by others using the conceptual framework of major transitions (e.g., [2,5,21]). Similarly, the empirical study of conflict and cooperation among genes has a long history and stretches back over 100 years (see [22] for a historical overview). Again, although these studies were not always interpreted within the framework of social evolution, it has long been clear that this can be done [3,5,23,24].

Empirical studies of evolutionary transitions

Recent years have seen a rapid influx of whole-genome data thanks to advances in high-throughput sequencing

(reference genomes are now available from over 160 eukaryotic and over 2200 bacterial species; <http://www.ebi.ac.uk/genomes/>) and this has led to the suggestion that the wide-reaching effects that genomic conflict may have on genome evolution remain underappreciated [25]. A particularly well-studied form of genomic conflict, and one where understanding has benefited greatly from whole-genome sequencing, is that between transposable elements and the rest of the genome (see below; Figure 2). Here, I review recent work on transposable elements in the light of evolutionary transition theory and argue that transposon data offer a rich empirical resource for the study of the second stage in the evolutionary transition in individuality, the maintenance of social groups. To that end, I first discuss the biology of transposable elements and theoretical underpinnings of mechanisms for social group maintenance. I then argue that the study of transposons may improve understanding of two fundamental questions related to the maintenance of individuality. First, the observed reduction in transposon abundance in highly selfing and asexual lineages provides clues to the circumstances under which the fitness interests of lower and higher levels may align. Second, improved understanding of evolutionary and ecological processes that affect the epigenetic control of transposon activity may help understand what prevents selfish behaviour at a lower level from disrupting functionality at higher levels. Finally, I suggest that, although the concept of evolutionary transitions provides a useful framework to interpret transposable element data, empirical insights from studies of transposons may in turn help improve the conceptual framework itself.

The biology of transposable elements

The assumption that genomes function as integrative cooperative units has a long tradition in biology [26,27]. However, conflict among genes not only is possible, but is also a dominant feature in eukaryotic genomes [22,28]. Selfish genetic elements are genes that have the ability to promote their own transmission at the expense of other genes in the genome (the genome here being all the genetic material of an organism) [29]. This results in conflict and the spread of selfish genetic elements often leads to selection for modifiers, which are other genes in the same genome that have evolved ways to counter this spread [30,28].

Genomic conflicts are remarkably diverse [22,30–32]. Arguably the most successful form of selfish genetic

Table 1. The major transitions in evolution and individuality

Event		Major transition sensu [5]	Evolutionary transition in individuality
From	To		
Replicating molecules ^a	Populations of molecules in compartments	Yes	Yes
Independent replicators ^a	Chromosomes	Yes	Yes
RNA as gene and enzyme	DNA + protein (genetic code)	Yes	No
Prokaryotes	Eukaryotes	Yes	Yes
Asexual clones	Sexual populations	Yes	Maybe (see [3,86] for discussion)
Protists	Animals, plants, fungi (cell differentiation)	Yes	Yes
Solitary individuals	Colonies (nonreproductive castes)	Yes	Yes
Primate societies	Human societies (language)	Yes	No
Independent species	Interspecific mutualism	No	Yes

^aThese are sometimes grouped together as one transition.

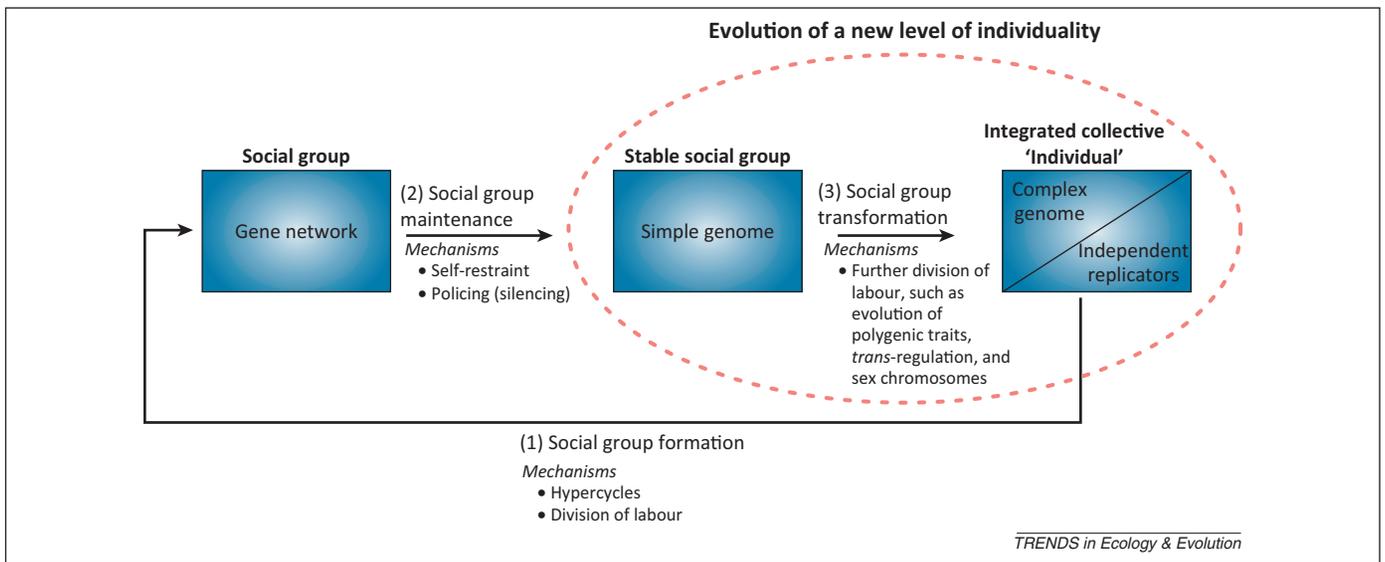


Figure 1. The three stages of an evolutionary transition in individuality [3], as applied to the origin of the genome. First, social group formation is the origin and spread of social behaviour in a population. At the genome level, this involved the first cooperative gene-networks and the beginning division of labour among genes. Second, social group maintenance are the processes that enable the social group to persist in a stable way. As explained in the main text, the stability of the genome is maintained through self-regulation and policing. Third, social group transformation is the origin of a new level of individuality. This involves further division of labour, including but not limited to, traits encoded by more than one gene, evolution of genes regulating expression of near (*cis*) and distant (*trans*) genes, as well as the evolution of chromosomes with sex-specific functions. Modified, with permission, from [3].

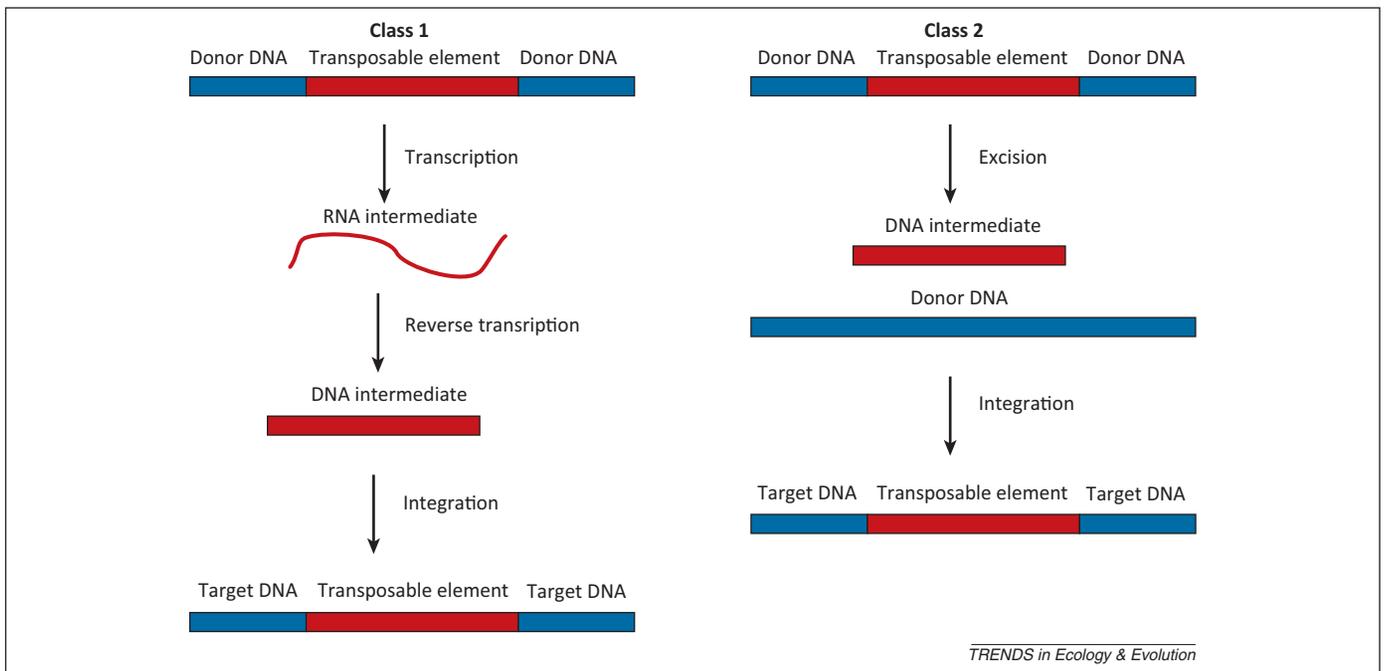


Figure 2. Transposable elements are typically divided into two classes depending on their method of self-replication [88]. Class 1 elements, sometimes known as retrotransposons, apply a 'copy-and-paste' mechanism and produce an RNA intermediate that is then reverse-transcribed into DNA and integrated into a new location in the genome. However, class 2 DNA elements replicate via a 'cut-and-paste' approach and the transposon is physically excised and integrated elsewhere in the genome. The movement of transposons has been suggested to be deleterious for three reasons [89,90]: (i) new transposon insertions end up in or near genes [91]; (ii) ectopic recombination between nonhomologous elements cause chromosomal rearrangements [92]; and/or (iii) metabolic costs imposed by the process of transposition itself [93].

elements is transposable elements, which are mobile genetic elements that can self-replicate and produce copies of themselves that may insert elsewhere in the genome (Figure 2). This movement is often associated with mutational effects and, therefore, creates a conflict between transposons and the rest of the genome [33]. Yet, transposons are the most common kind of genetic material [34] and comprise >80% of the genomes in some species but are

almost absent in others [35]. Therefore, examining the evolutionary forces that enable transposons to proliferate so successfully in some species, but not in others, can provide a window on an ongoing genomic conflict and its resolution.

Mechanisms of social group maintenance

Despite the potential for widespread conflict introduced by transposons, the genome does not implode, which suggests

that there is a force(s) holding the group together. All levels of individuality are vulnerable to selection at lower levels favouring selfish behaviour [2,3,5] and two routes to social group maintenance have traditionally been considered [36]. First, if the fitness interests of lower and higher levels are aligned, self-restraint of selfish behaviour is expected to evolve, because the only way to maximise fitness at one level is to maximise it at the other level. Alternatively, cooperation may be promoted by the active suppression of conflict [37,38]. One such mechanism is the forcible prevention of selfish behaviour through policing. Here, the opportunity for cheating is removed and the only way to maximise individual fitness is by maximising group fitness. Policing can enforce cooperation by aligning the fitness interest of interacting entities and so make the group act as one cohesive functional unit. Below, I expand on how these mechanisms may play out at the genome level and discuss how recent studies on transposons suggest the action of both self-restraint and policing in maintaining cooperation in the genome.

Self-restraint in the genome

Both theoretical and empirical work suggests that the mating system will have an important role in aligning the fitness interest of genes with those of higher levels of the organisation. Highly selfing or asexual species are expected to experience a reduction in intragenomic conflict for several reasons [39–42]. Considering the conflict between transposons and the rest of the genome, a particularly important difference between selfing and asexual lineages on the one hand and outcrossing lineages on the other is the extent of linkage disequilibrium in the genome. Linkage disequilibrium is the nonrandom association of alleles at two or more loci (i.e., a measure of how likely two genes are to be inherited together). This association may favour cooperation among these genes. Thus, it is conceptually analogous to an iterated prisoners dilemma and, therefore, one may expect linked genes to show greater cooperation than unlinked ones [29,43,44]. The reduction of linkage disequilibrium in outcrossing genomes means that the association between a given transposon and any deleterious mutational effects that it may have is more likely to be decoupled by recombination. Therefore, the transposon can more easily spread in an outcrossing population, compared with a selfing or asexual population, where higher linkage disequilibrium leads to a stronger association between transposons and their deleterious effects. As a consequence, one may expect transposons showing self-restraint to be more common in selfing compared with outcrossing lineages [45].

Empirical support for the role of the mating system in social group maintenance in the genome comes from a variety of systems. First, few transposons are present in the ancient asexual bdelloid rotifers, but common in their sexual relatives [46]. Stronger evidence comes from species that vary in their mode of reproduction. For example, populations of the water flea *Daphnia pulex* can be either cyclical parthogens ('sexuals'), which during the growth season reproduce asexually and then switch to sexual reproduction in response to seasonal signals, or, alternatively, completely asexual. Schaak *et al.* [47] compared the

abundance of transposons in sexual and asexual populations, finding that the sexuals harboured more transposons than did the asexuals. Evidence that sex may promote the spread of genomic conflict has also been obtained experimentally. For example, when infected with a novel transposon, rapid spread was observed in sexual but not asexual strains of yeast [48]. Finally, the selfing plant *Arabidopsis thaliana* has fewer transposons than its outcrossing relative *Arabidopsis lyrata* [49] and there is evidence suggesting that this is due to the accumulation of transposons in the outcrosser, rather than loss in the selfer [50].

Alternative strategies for transposons

The above argument assumes that transposons are deleterious and persist in genomes thanks to their selfish behaviour. An alternative strategy for a transposon would be to adopt the same approach that many other genes do, that is to work with other genes to promote whole-organism-level fitness. Arguments that transposons may provide adaptive benefits at the organism level have a long history [33,51], and recent studies suggest that examples of transposon-induced adaptations do exist, not only in bacteria, but also in eukaryotes [52,53]. Thus, an important avenue for future work should be to determine how common this is [54]. However, the evidence to date is overwhelmingly in support of the hypothesis that transposons are predominantly associated with fitness costs, and that their maintenance in populations is due to their ability to transpose despite these costs [55,56]. Thus, even if beneficial transposon insertions occur, most insertions are likely to pose a threat to the maintenance of genome integrity.

Policing the genome

The enforcement of cooperation through policing has long been recognised as a likely important factor in driving evolutionary transitions [10,37,57,58]. Although understanding of policing mechanisms has made great progress through studies on whole organisms, in particular social insects [59], the first articulation of the argument that conflict suppression could promote cooperation was made in reference to fair meiosis [60]. Furthermore, it has long been recognised that several features of the genetic system appear to be adaptations to reduce conflict among genes. Examples of this include randomised segregation during meiosis [24,61], enclosing genes in cells [5,62], organising genes in chromosomes [5], and the uniparental inheritance of organelle genomes [29]. Still, until recently, technical limitations made the genome the most inaccessible of all hierarchical levels at which to study cooperation empirically and understanding of the molecular mechanisms of policing at the gene level remained limited.

Empirical examples of transposon policing

Over the past few years, improved understanding of policing of transposons has been instrumental in changing this picture. It is now known that, in most genomes, most transposons are not actively transposing at high rates, because their mobility is downregulated through several mechanisms [63]. Transposons are typically epigenetically silenced by a variety of small interfering RNAs (siRNAs). These siRNAs are then incorporated into a larger protein

complex, which either destroy transposon transcripts or target transposon sequences with chromatin modifications or DNA methylation, thus preventing the transposon from transposing [64].

The relation between transposons and their silencers can be viewed as an example of antagonistic coevolution between selfish genetic elements and their modifiers. This arms race is often rapid and, therefore, different populations may fix for different sets of selfish genetic elements and modifiers. As a consequence, when individuals from different populations or species interbreed, the offspring may suffer from increased levels of intragenomic conflict due to a mismatch of inherited selfish genetic elements and modifiers [65]. A good example of this is the experimental cross between *A. thaliana* and *Arabidopsis arenosa*, which results in elevated expression of *ATHILA* transposons in the hybrid [66]. Similarly, crosses between two species of Australian wallaby (*Macropus eugenii* and *Wallabia bicolor*) led to a large increase in the size of centromeres due to proliferation of retroelements [67]. Finally, because of proliferation of the *Ty3/gypsy* retrotransposon, the three *Helianthus* sunflower species *H. anomalus*, *H. deserticola*, and *H. paradoxus*, all products of the same hybridisation even between *Helianthus annuus* and *Helianthus petiolaris*, have genomes that are approximately 50% larger than that of either parental species [68].

Efficiency of transposon policing

What may determine how efficient transposon policing is? There is growing evidence that the policing of transposons comes with a fitness cost, because the silencing of transposons can also affect the expression of nearby genes [69]. Yet, at any given time and in most genomes, most transposons are actively silenced [70]. Thus, the integrity of the genome appears highly contingent on the efficacy of the silencing system, and the ongoing maintenance of genomic conflict may be driven in part by location-specific costs of silencing. Furthermore, the ability of the immune system to deal with antigens is weakened when the body is under stress and the same seems to be true for control of transposons. Examples of stresses that have been linked to increased transposon expression include infections by bacteria and fungi, wounding, high and low temperatures, and water availability [71,72]. Thus, changes in both the genomic and external environment may result in the breakdown of transposon silencing. Taken together, these observations of genomic consequences of silencing breakdown highlight the importance of policing to the maintenance of genome integrity.

Social group maintenance in the genome

How much of a threat did transposons present to early genomes? Although transposons occur primarily in (sexually reproducing) eukaryotic genomes, they are also found in prokaryotic genomes. Furthermore, both self-regulation [73] and policing [74] appear to have some role in regulating their activity. Durand and Michod [75] recently applied empirical examples from studies of transposable elements to Eigen and Schuster's [18] theoretical models of hypercycles of replicators to elucidate the early stages of the formation of the genome as a social group. They argued

that the division of labour between genes influencing viability and reproduction, respectively, was key to both the formation and transformation of the genome as a level of individuality. However, they also pointed out that to understand the origin of the genome fully, one must also understand what prevents conflict from arising among the genes constituting the genome. That is, what governs the maintenance of social groups at the genome level (Figure 1)? The well-developed literature on evolutionary transitions provides a solid conceptual framework to address this question using the large amounts of genomic data on transposable elements currently being generated.

Reciprocally, these new empirical observations may also stimulate the further development of the current conceptual framework of transitions in individuality. Michod [76] argued that the full decoupling of fitness from lower levels is required before the evolution of a new level of individuality is complete. Therefore, conflict at lower levels must be (almost) completely suppressed; other authors have reached similar conclusions [77]. Whereas self-fertilising and asexual lineages are expected to experience less genomic conflict, most multicellular organisms, including plants, are outcrossing [78]. Thus, a given level in the hierarchy can still function despite extensive conflict at lower levels, consistent with the growing consensus that the argument that complete transitions in individuality require the total suppression of conflict at lower levels is too stringent [6,79]. Moreover, the demonstrated importance of silencing of transposons in maintaining genome unity suggests that policing, although having a minor role in some transitions [38], may be more important than previously anticipated in others. Thus, although the same principles appear to operate at different levels in the hierarchy, their relative importance may vary, and the only way to test this will be to apply theoretical models to new data [4].

The future of social evolution is in the genome

There is currently an emerging synthesis marrying social evolution, the theoretical backbone of studies of evolutionary transitions, with genomics [12,80,81]. This synthesis has two fruitful outcomes. First, it means that the genetic architecture of social behaviour is no longer beyond reach [82]. A second, perhaps less appreciated, outcome is that it, for the first time, enables researchers to explore fully the extent to which the theoretical framework of social evolution can be applied to the evolution of genome architecture. As illustrated in this paper, the potential for this second outcome is promising.

Now is a particularly good time to explore the second outcome. In 1983, Stephen Jay Gould [83] asked: 'How much repetitive DNA is self-centered DNA? If the answer is "way less than one percent" because conventional selection on bodies almost always overwhelms selection among genes, then self-centred DNA is one more good and plausible idea scorned by nature. If the answer is "lots of it," then we need a fully articulated hierarchical theory of evolution'. One need not embrace Gould's particular version of a hierarchical theory to recognise that, 30 years on, improved understanding of genome architecture leads to a resounding confirmation of the "lots of it" alternative [34].

In other words, there are almost endless amounts of data that can be approached with the tool kit of social evolution. As has been pointed out elsewhere [3], the application of the ideas of social evolution to entities below that of the individual is still restricted to a few enthusiasts (e.g., [4,12,23,84]).

Concluding remarks

Issues surrounding conflict and cooperation in a hierarchical setting and evolutionary transitions in individuality can be organised around two questions: (i) under what circumstances are the fitness interests of lower and higher levels aligned?; and (ii) what prevents selfish behaviour at a lower level from disrupting the functionality of higher levels? Here, I have reviewed empirical evidence from studies of transposable elements that can be interpreted in the evolutionary transitions framework. Transposable elements are just one example of genomic conflict; the broader genomic conflict literature offers a gold mine of data to further examine the social interactions that occur within the genome. Comparisons between the organisation of multicellular organisms and societies date back a long time [85] and it is now time to take the final step and integrate the genome, and the empirical resources of genomics, into the general theory of social evolution and the study of evolutionary transitions in individuality.

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