Evolution and impact of socially transferred materials

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Keywords

Allohormones, metabolomics, parental care, physiology, seminal fluid, microbiome

Highlights

- Animal behavior is influenced by interactions with conspecifics. Quantitative genetic models that include indirect genetic effects arising from these interactions show that they can strongly drive evolution.
- Through socially transferred materials, the influence that one individual has on others can be analyzed quantitatively and from a molecular perspective.
- Recent advances in molecular biology and behavioral ecology allow for the first time the measurement of precise physiological and behavioral effects of these transfers.
- Our synthesis, drawing from interacting phenotype models, the inclusive fitness framework, game theory and signal theory, provides the necessary conceptual framework for understanding both the proximate and ultimate roles of socially transferred materials in social evolution.

Abstract

Since the dawn of life, transfers of metabolized material between individuals have led to great innovations of evolution. When metabolized material is transferred from one individual's body to another (as with sperm, eggs, milk, symbionts), secondary manipulative molecules that induce a physiological response in the receiver are often transferred along with the primary cargo. The bioactive and transfer-supporting components in these socially transferred materials have evolved convergently to the point where they can be used in applications across taxa and type of transfer. Because these materials' composition is typically highly dynamic and context-dependent, their focused study will allow deeper understanding of their transformative evolutionary and physiological role. We synthesize a conceptual framework for their study, and discuss future directions.

Molecules transferred between individuals are fundamental in social evolution

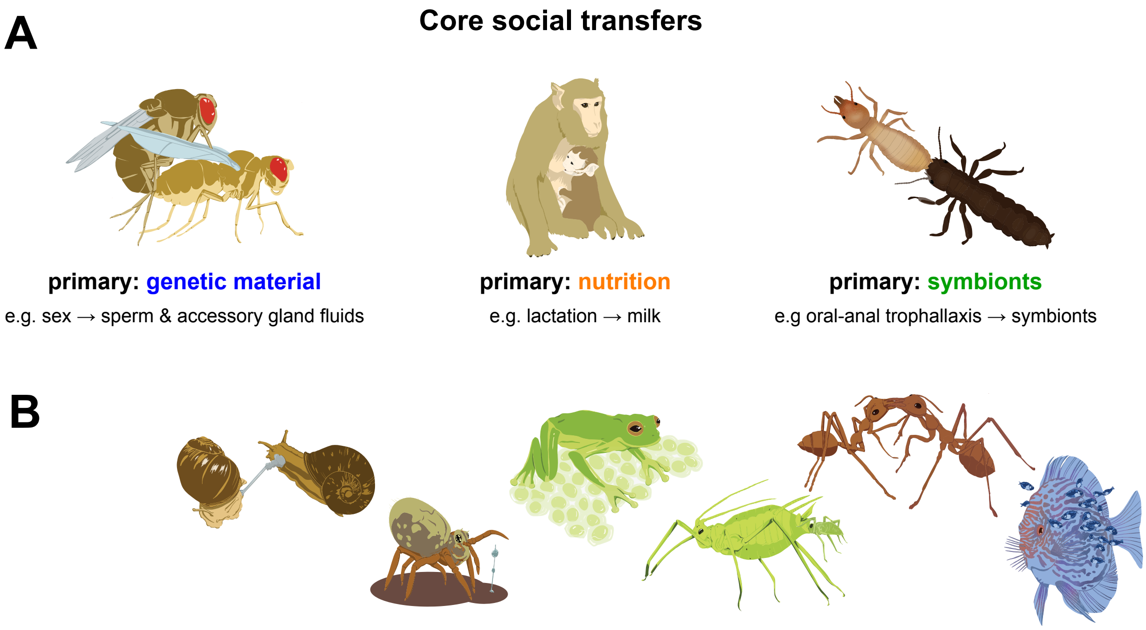
All animals interact with other individuals of their own species at least some point in their life. They communicate with visual, chemical and auditory signals evolved for this purpose and use indirect cues to gain information [1]. In addition to these well-studied means of communication, animals have also evolved behaviors where biological material is passed from one individual's body to another and interacts directly with their physiology, bypassing sensory organs.

Socially transferred materials (see Glossary, Box 1, Figure 1) are usually associated with highly fitness-relevant contexts, such as mating in the case of ejaculates [2,3], or parental care in the case of egg yolk and milk [4–7]. **Social transfers** like these open a direct channel between individual bodies, and thus their transferred materials can have strong impacts on the physiology of the receivers, making them evolutionarily more important than currently appreciated. Even though material transfers between conspecifics have been reported for hundreds of years across multiple taxa, only a few are well-studied, and many of the molecular mechanisms in even these flagship transfers are still poorly understood.

Socially transferred materials may fill an important gap in our understanding of social evolution. The interacting phenotypes framework has proven useful for modeling and empirically studying the evolution and genetic architecture of traits involving social interactions [8–11]. This framework considers how an individual's phenotype is directly affected by its own genotype and indirectly affected by its social partners' genotypes. As such, it has been used to identify genes and alleles underlying variation and expression of socially-influenced traits [12–14]. Apart from these recent studies, this framework has mostly treated the mechanistic details by which genes influence social traits as a black box. Importantly, socially transferred materials are likely to play central functional roles in these mechanisms. Approaches that explicitly study them can help bridge the gap between mechanistic understanding and eco-evolutionary dynamics of the interacting traits and genes.

Socially transferred materials have commonalities in their components and modes of production, transmission and uptake, despite the diversity of impacts they exert on receivers. They allow resources acquired by one individual in one time and place to be used by another individual in another time and place. Their components (Table 1) range from structural and nutritional building blocks such as fatty acids, amino acids and carbohydrates, to complex molecules like proteins, RNA or antibodies functioning as allohormones [15], all the way to fully functional cells [16–22]. Socially transferred materials can have long-lasting effects on the receiver, for example, affecting an individual's development or long-term health [23–26]. Additionally, they also have short-term impacts on behavior and physiology [27–29]. Socially transferred materials can disperse horizontally among individuals (as in [5], or be transferred vertically between parents and offspring [7,23,30,31]. Currently there is no comprehensive theoretical framework for studying the evolution and impact of all socially transmitted materials together.

The aim of this review is to define social transfers and the materials they transmit (Box 1, Figure 1), highlight the commonalities across them (Table 1), describe how they can be best studied at both proximate and ultimate levels, discuss their potential for applications, and bring together and further develop the theoretical frameworks that best aid in understanding their evolution and the indirect genetic effects they impose. This uniting conceptual framework will benefit each individual research domain through overarching theory down to molecular pathways.



Primary cargo	genetic material	genetic material	genetic material nutrition	nutrition	nutrition	nutrition
Social transfer	***love darts***	***spermatophores***	***eggs***	***viviparity***	***trophallaxis***	***mucus***
Partner relatedness	*low*	*low*	*high*	*high*	*high*	*high*
Separation in time	*synchronous*	*asynchronous*	*asynchronous*	*synchronous*	*synchronous*	*synchronous*
Rate and duration	*one-time, brief*	*one-time*	*one-time*	*one-time, sustained*	*frequent, sustained*	*frequent, sustained*

Figure 1: Examples of socially transferred materials in animals

A: The three main classes of socially transferred materials based on the primary transmitted cargo: genetic material, nutrition, and symbionts. Note that although this review focuses on animals, the same principles and classifications can be applied for other organisms as well.
B: Examples of socially transferred materials, with suggestions for classification based on relatedness of partners (e.g. parent to offspring → high relatedness), whether the material is deposited at the same moment as it is consumed (synchronous) or these are separated in time (asynchronous), and the rate and duration of the social transfer. Synchronous transfers can allow for bidirectional transfer of material.

BOX 1: Definition and scope of socially transferred materials

- ***Socially transferred materials*** *are transferred between conspecifics and i) include components metabolized by the donor, ii) which induce a direct physiological response in the receiver, bypassing sensory organs, and iii) benefitting the donor.* This definition is built on the definition of **allohormones** [15], and broadened to include the transfer of functional cells, and transfer to and from individuals that are not free-living, such as offspring developing inside the parent or anglerfish males living inside the females [32], because the only route to the evolution of non-free-living individuals is via social transfers. A key distinction to separate socially transferred materials from pheromones is that components of socially transferred materials directly interact with the receiver's physiology, bypassing sensory organs. The materials can, however, additionally include pheromonal components.

- ***Social transfers*** *are the behaviors that evolved to transmit socially transferred materials.* Mere foraging or preparation of food for other individuals are not social transfers, unless the donor adds metabolized substances that target recipients.

- Socially transferred materials typically consist of different components that are governed by different selection pressures, some social and others biophysical. Social transfers require a ***vehicle*** that enables the transmission of the primary cargo, such as ejaculate to transmit genetic material, egg, milk, or mucus to transmit nutrition, or adapted forms of feces to transmit symbionts. The *primary cargo* or ***primary component*** *that is transferred*, such as nutrition, genetic material, or symbionts, is the evolutionary motivation for the transfer – the main cargo the vehicle carries. Over evolutionary time, this primary component is supplemented with ***secondary components*** that often function as allohormones to manipulate receivers, or have stabilizing and preserving functions for the whole vehicle or for some of the components.

- Care behaviors such as grooming may transfer allohormones, and as such, can be social transfers. In these cases, the vehicle (such as saliva or sweat) did not originally evolve to be transferred. These kinds of materials can function as stepping stones towards more complex socially transferred materials, as the evolution of lactation shows [4] (Figure 2).

- The behavioral context for social transfers is typically specialized, and often involves highly adapted physiological features such as glands that produce and secrete the transmitted components. In some cases, full organs have evolved for these functions, such as penises, love darts, spermathecas, placentas and nipples.

- Socially transferred materials are inherently targeted, but they can be asynchronous in time. The excretion, secretion or regurgitation by the donor can be dissociated in time from the recipient's uptake of the socially transferred material, as for example in many taxa of soil invertebrates where males leave spermatophores for females to find [33,34].

- Finally, social transfers can be more or less frequent or sustained (Figure 1), ranging from a single brief event all the way to the shared physiology of placental viviparity, or an ant colony connected by the social feeding network of **trophallaxis** [24,35,36].

Classification of socially transferred materials

Social transfers can be classified in many ways (Figure 1), but one of the most informative is to classify them according to their *primary components*. We identify three main classes of basal transfers: the transfers of genetic material, nutrition, and symbionts.

Basal transfers of genetic material include vertical transfers from parents to offspring, and horizontal transfers between the parents. In the vertical transfer, in addition to genetic materials, ovules and sperm often carry non-coding components that can exert epigenetic control over the offspring [37–42]. Many of these vertical transfers act out the conflicts between parental genomes and conflicts between parents and offspring [43]. In some cases, sex-related social transfers are a stepping stone to care-related transfers (e.g. eggs containing also nutrition, such as yolk).

In the horizontal transfer between mating partners, many secondary components in ejaculate and female reproductive fluids play major roles in sexually antagonistic arms races [44–46]. Products transferred between partners during courtship range from nuptial gifts of exogenously or endogenously sourced food [47–49], to mating plugs controlling female behavior [50], all the way to sexual cannibalism where the receiver eats the donor [51]. In some animal taxa, mating involves the partners attaching to each other for shorter or longer time periods – or even permanently with a shared blood flow as in some anglerfish species [32]. The tighter the association, the greater the risks taken in opening a direct channel between bodies (discussed in detail in the next section).

Basal transfers of nutrition are most commonly related to parental care, which in its most ancient form is provisioning offspring with nutrition in or around the eggs. This evolutionary innovation allows the parent to not just transfer nutrition to their offspring but also to metabolize it into suitable format for them, and to preserve it to be used later in time. In addition to nutrition, there are many examples where egg molecular composition and allohormones impact outcomes such as hatching order, physiology or success of offspring [52–54]. Additionally, care-associated materials can be deposited outside porous soft-shelled eggs [42], secreted or excreted by glands in synchronous or asynchronous transfers [5,31], offspring can cannibalize their siblings or even the parents [51,55,56], or the parent can lay trophic eggs for offspring to eat [57]. Mucus is used for feeding offspring in many aquatic taxa [58–60], and many animals have even evolved specialized feeding organs such as mammary glands or larval tubercles [61,62]. All forms of viviparity likely include social transfers, from invertebrates like tsetse flies to eutherian mammals with their highly specialized placentas [63,64].

Care-based transfers of nutrition often target offspring, but material can also be transferred horizontally to relatives or other members of social groups. These transfers can transmit donor-produced molecules orally through saliva during feeding or grooming [65,66], or through regurgitate [35,67–69]. In the case of some social insects that engage in mouth-to-mouth trophallaxis very frequently, this creates a social circulatory system that essentially generates a shared physiology at the level of the social group [5,35].

Basal transfers of symbionts are likely rarer, but accumulating evidence suggests that the microbiome and other symbionts are of such importance to the physiology of animals that specific behaviors for transferring them must have a larger evolutionary role than historically considered. However, so far the secondary components in such transfers have received little to no study, apart from a few main examples such as the termite microbiome transfers [70]. Symbionts, and molecules supporting symbiotic relationships, can also be components of all the other socially transferred materials, and be transmitted for example in oral regurgitation [23,71,72], anal excretion [73], mucus [74], feces [75], symbiont capsules [73], to the offspring via the egg [76], during internal insemination between the mating partners [77], or in viviparous animals through direct contact between offspring and parent [78–80]. While we classify mammalian milk as being a nutritional transfer, it has been hypothesized that early versions of milk may have evolved to regulate bacterial communities [4]. Indeed, many of the complex oligosaccharides in human milk appear to be nourishment for specific bacteria that need to colonize the newborn digestive tract [81].

Convergent evolution across socially transferred materials

The vehicles that enable social transfers (see Figure 1) are generally composed of a slew of different chemical and genetic components. In many cases, components have similar molecular functions, even in completely different socially transferred materials and across taxa (Table 1). Ultimately this is because similar selection pressures – costs, benefits, and fundamental physics and chemistry – shape the evolution of these transfers, regardless of their behavioral context. The constant evolutionary balance between cooperation and conflict can push the socially transferred materials to evolve to be increasingly complex, and induce further evolutionary changes in the whole organism (Figure 2, further discussion in Concluding Remarks).

Among the most consistent selection pressures for the composition of socially transferred materials are the multiple risks of opening a direct physiological channel between bodies, as happens in social transfers (e.g. [82]). For example, opening such a channel introduces significant potential for infection – sexually transmitted diseases are emblematic of this risk. Reflecting this infection risk, the secondary components in socially transferred materials are often defense-related: antibodies, antioxidants, DNAses, RNAses, antimicrobial proteins and peptides, and even immune cells [83]. These can function to protect the transferred materials (e.g. [84]) or be used to enhance the defense system of the recipient [21,30]. Especially when the transfer is recurrent or sustained, the level of risk is high (e.g. placental viviparity can bring about problems like gestational diabetes when physiological control mechanisms are compromised [85]), but is balanced by the high benefits and common interests between partners of these interactions.

An important class of secondary components in socially transferred materials are stabilizing molecules enabling the transfer of other molecules. Many of these may be convergently present in socially transferred materials across lineages. For example, protein families involved in RNA or lipid transport, or antioxidant activity, have been found across many socially transferred materials. In honey bee royal jelly, MRJP-3 protein plays a key role in concentrating, stabilizing, and enhancing RNA bioavailability, facilitating social immunity and signaling among bees [86]. In an even more complex case, a recent study in the plataspid stinkbugs shows that females deliver essential symbionts to offspring via capsules laid simultaneously with the eggs, and a specific protein is responsible for stabilizing the symbiont in them [73].

Orthologous genes in vastly different lineages are often co-opted for use in social transfers either to ensure chemical stability and preservation, to transfer components, or to alter recipient physiology. Many molecular parallels can be found between proteins in *Drosophila melanogaster*'s seminal fluid and regurgitate transmitted mouth-to-mouth in ant colonies, including esterase-6/juvenile hormone esterase, serpins, serine proteases, regucalcin, transferrin, lectins and some uncharacterized but orthologous proteins [20,35,87]. Likewise, potentially bioactive proteins can be repurposed from known protein families with different functions. For example, an allohormone transferred in the mucus on the love dart of land snails shows resemblance to a known neuromodulator peptide buccalin that modulates muscle contractions in other gastropods [29].

Even across distant taxa, molecular commonalities can be observed – the nutritive fluid that ants feed to their colony members has molecular commonalities with mammalian milk, namely the abundant proliferation protein CREG1, many lipoproteins or fatty-acid binding proteins, and antioxidant enzymes like xanthine dehydrogenase and superoxide dismutase [18,35,88]. In most cases, protein function is unclear, but in some cases it can be deduced. For example the protein tetraspanin is found in most socially transferred materials and is an established marker of exosomes (extracellular vesicles) [89], a major mode of cargo transmission between cells. Its presence across social transfers indicates that exosomes are also used to enable transfers between individuals.

Many socially transferred materials also share similar response dynamics: their composition changes with the social and environmental context and individual condition [90–96]. This dynamic and highly responsive nature is likely an important aspect of all socially transferred materials, and may enable more rapid adaptation. In addition to the donor-induced plasticity in the socially transferred materials, it is likely that receivers' responses are equally plastic, adding further dynamicity to these interactions.

Table 1 (next page): Commonalities across socially transferred materials.

The molecular composition of socially transferred material has evolved convergently in different socially transferred materials and across taxa, as the selected examples show. Although some social transfers have clearly evolved around the basal transfer of symbionts [70]*, there is substantially less research done on them and they are thus not included as a main category here. However, symbionts are common in most socially transferred materials, and are thus mentioned as secondary components. Abbreviations: Female reproductive fluids (FRF), xanthine dehydrogenase (XDH), superoxide dismutase (SOD), glucose dehydrogenase (GluDH), juvenile hormone (JH), heat shock protein (HSP).*

		Genetic material		Nutrition	
		Vertebrates	Invertebrates	Vertebrates	Invertebrates
Basic building blocks	**Sugars**	Ejaculate [97]	Ejaculate [98]	Milk [30], [26] e.g. simple sugars, complex oligosaccharides Regurgitate [23]	Eggs [99] Regurgitate [100]
	Free amino acids	Ejaculate [97]	Ejaculate [97]	Milk [26]	Regurgitate [99] Excreta [101]
	Lipids Fatty acids Triglycerides	Ejaculate [102], [103], [104] e.g. cholesterol, glycosphingolipids, prostanoids	Ejaculate [105]	Saliva [66] Milk [30], [26] e.g. fatty acids, gangliosides, cholesterol Regurgitate [23] Eggs [106] e.g. yolk lecithin, alkaloids	Eggs [99] Regurgitate [90] e.g., cholesterol, fatty acids, long-chain hydrocarbons
	Vitamins & minerals	Ejaculate [107] Ejaculate [103] e.g. vitamin D		Milk [30], [26] e.g. Magnesium, iron, calcium, Vitamins A, D, E and K Regurgitate [23] Mucus [58] e.g. calcium	
Hormones	**Hormones**	Ejaculate [103] e.g. Steroids, cortisol, renin, angiotensin	Ejaculate [97], [3] e.g. Lucibufagin, JH	Saliva [65] e.g. Ghrelin Eggs [108], [109] e.g. Steroid & thyroid hormones, Cortisol Mucus [58] e.g. Cortisol	Regurgitate [90], [5] e.g. JH, vitellogenin Eggs [99] e.g. JH, vitellogenin
RNA	**Small/non-coding RNA**	Ejaculate [110], [111], [112]	Ejaculate [113]	Milk [30] Saliva [111]	Eggs [99] Regurgitate [90]
	Nucleotides	Ejaculate [97]	Ejaculate [97]	Milk [26]	
Proteins		Ejaculate [103], [114] e.g. immunoregulatory factors, cytokines FRF [115]	Ejaculate [116], [28], [105], [3], e.g. transferrin, est-6, serine proteases, serpins, OBPs Injection devices [119], [29], [120], [121], [84] FRF [122] e.g. apolipophorins, transferrin, PPO, GluDH, HSPs, cathepsins, OBPs, est-6	Milk [30] e.g. Casein, transferrin, a- γ- β-globulin, albumin, lysozyme, cathelicidins, XDH, CREG1, tetraspanin Eggs [106] e.g. Ovoalbumin, ovotransferrin, ovoinhibitor, avidin, cystatin, vitellogenin, lysozyme Mucus [58], [59] Regurgitate [23] Saliva [59]	Eggs [123] e.g. vitellogenin Regurgitate [90], [35] e.g. GluDH, apolipophorins, hexamerins, cathepsin, vitellogenin, CREG1, amylase, major royal jelly proteins, JH esterases, transferrins, serine proteases, serpins, OBPs, cathepsins, HSPs, XDH, SOD
	Antibodies & Anti-microbials	Ejaculate [124], [63] FRF [118]	Ejaculate [118]	Eggs [106] e.g. IgY Saliva [125] e.g. IgG, IgM, IgA Milk [30], [126] Mucus [58] Regurgitate [23]	Regurgitate [90]
Cells	**Symbionts**	Ejaculate [118] FRF [118]	Ejaculate [77]	Mucus [74] Regurgitate [23]	Eggs [127] Regurgitate [71], [72] Excreta [73], [128]
	Immunity cells	Ejaculate [97]	Ejaculate [97]	Milk [30] e.g. Neutrophils, lymphocytes, macrophages	
	Other cells	Ejaculate [97]	Ejaculate [97]	Milk [30] e.g. stem cells	

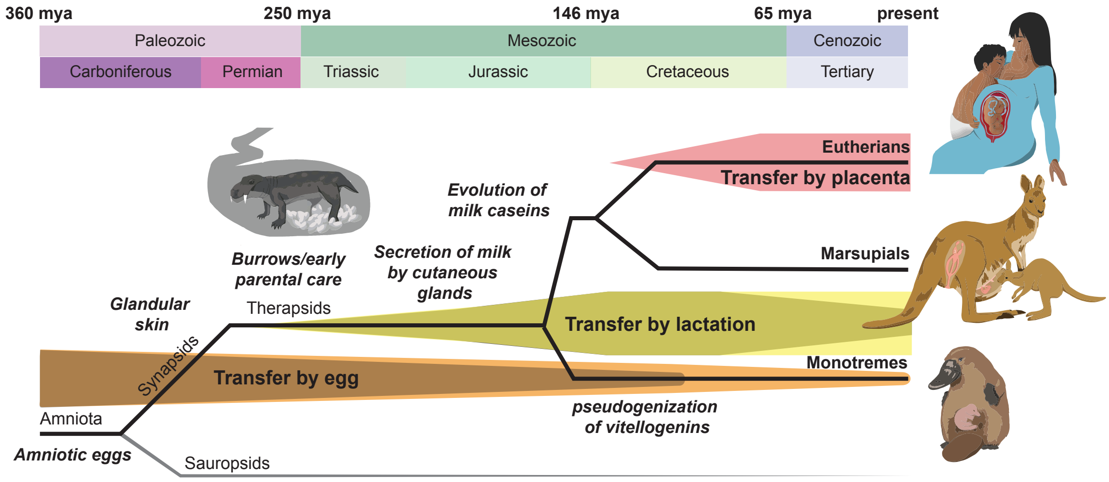


Figure 2: Evolution of nutrition-related socially transferred materials in mammals

Socially transferred materials are key innovations in evolution. During the course of mammalian evolution, different types of vehicles, behaviors and genes have replaced each other under the selection for better nutrition, care and control over offspring. The amniotic egg was an evolutionary innovation that allowed for greater maternal provisioning through the egg. Synapsids evolved glandular skin, a critical pre-adaptation that would go on to be necessary for the evolution of milk [4,61]. *Therapsids laid their eggs in a burrow and provided parental care* [129], *another important pre-adaptation. Over the approximately 100 million years from then until the most recent common ancestor of extant mammals, milk evolved to be secreted by highly adapted cutaneous glands. This may have been for the sake of nutrition, but alternatively, it may have been to regulate moisture, temperature and/or bacterial communities around the eggs and offspring* [4]. *Now all extant mammals rely on milk in their development. This required the evolution of secretion pathways, glandular tissue and genes like the caseins that evolved to be the major nutrient transfer components of milk* [4]. *This decreased the need for egg-derived nutrition – the three vitellogenins, major nutrient transfer components of egg in both vertebrates and invertebrates, became pseudogenes in mammals, with the exception of one that remains only in monotremes* [130]. *Milk in marsupials is extremely complex and variable over development, more so than the milk of eutherian mammals* [4]. *In eutherians, when the placenta evolved to allow extended viviparity, it took over many of milk's functions, even co-opting many of the same genes* [131]. *The decreasing importance of first egg-derived components and later milk-derived components in some of the lineages is represented by variable highlight colors.*

Stages and methods of research

Here we outline a concept of a research program that, if pursued across taxa and for multiple social transfers, will allow large-scale comparative analyses for the evolutionary role of socially transferred materials and their indirect genetic effects, and the selection pressures affecting their evolution in both donors and receivers.

Step 1: Establishing a social transfer and its impact on the receiver. Recognizing a behavior that passes allohormones along with primary components (genetic material, nutrition, symbionts) relies on traditional natural history approaches. In many taxa, social transfers were described decades ago, but were never studied further at the molecular level or in the evolutionary context – thus the study of socially transferred materials already has a strong foundation and rich literature to draw upon.

Step 2: Characterizing what is transmitted during the behavior. Comparative sequencing and transcriptomics, as well as metabolomic and proteomic studies are the first step to analyze the molecular content of transferred materials (for example [35,88,132]). Confirming which molecules originate in the donor instead of the receiver typically requires extra care in study design. To determine how donor-derived components arrive in the receiver and achieve their impacts, it is necessary to establish origin, processing and degradation. Histological methods such as *in situ* hybridization are useful for characterizing tissue-specific expression and localization [117], as are tissue-specific gene expression measures (qPCR, single-cell RNAseq [28], transcriptomics [133]) and mass spectrometry imaging techniques for tissue-specific translation [134]. Transfer of proteins can be further tracked by incorporating stable isotopes in essential amino acids into donors and monitoring proteins found in receivers [135]. Other metabolic labelling methods can incorporate nucleic acid derivates (e.g. thiouridine) to label RNA or click chemistry to label proteins, nucleic acids or metabolites and to detect their modifications [136]. Many of the newest techniques are only available in model organisms but recent innovations especially with CRISPR, sequencing technology, click chemistry and in the imaging and bioinformatic side of mass spectrometry, allow significant advances in non-model organisms too.

Step 3: Understanding context dependence. For each social transfer, the effects of social and environmental contexts and individual conditions should be correlated with molecules transmitted. This will help identifying the most interesting bioactive molecules for further investigation. Overall, current research regimes often do not inspect different environmental and physiological contexts to understand the dynamic nature of these materials, or inspect too variable contexts and end up diluting meaningful plasticity into noise around averages. Therefore, it is important to develop assays that consistently show shifts in the composition of the transferred material with context and condition. Because donor condition and receiver condition can have independent effects, tools like cross fostering or artificial insemination can be effective for disentangling impacts.

Step 4: Establishing the function of component molecules on receivers. To understand the importance of these transfers in the social life of the organisms, establishing molecular and physiological functions are necessary. This research step is multifaceted, because the impacts of single molecules on receivers are often context dependent [95,137] and hard to detect without controlled experimental paradigms. Single molecules may require the presence of other molecules in the vehicle, and thus with the current single molecule testing approach, some effects may be missed. Some previously mentioned methods for following the transfer routes of molecules can also reveal their functionality in receivers, but in many cases it is necessary to directly manipulate the molecules or their composition [28,87,138], or if possible, the underlying genes or biosynthesis pathways in donors, or receptors in receivers. Studying the target receptors or uptake of molecules in the receiver would be important to fully understand the intra-individual molecular pathways, but has proven to be difficult; although *D. melanogaster* seminal fluid proteins are well studied, and many of their functions have been established in females, only a single receptor has been characterized [139]. Finally, pairing the current revolution in automated deep-learning based behavioral tracking in behavioral ecology [36,140–142] with tracking of transmitted molecules will allow researchers to interpret the effects of social transfers, not only on physiology but also behavior, in a quantitative and high-throughput manner.

Step 5: Underlying genetic architecture. Once the socially transferred molecules have been identified, analysing the underlying genetic architecture of these molecules, genomes and behaviors become possible. Comparative genomics allows the study of socially transmitted molecules' evolutionary trajectories and could identify genomic changes associated with the evolution of social transfers. For example, recent studies show that some of these materials are not conserved but instead show fast expansions of key gene families [14,44,87,143,144]. Special care must be taken in assigning gene orthologs in such studies, as currently annotation based on model organisms such as *D. melanogaster*, *C. elegans*, or *M. musculus* is the norm due to very sparse characterisation of gene function in other taxa. This easily leaves the taxon-specific, fast evolving and novel genes unidentified, and creates a risk of misinterpreting their function. For example, M*egaponera analis* ants use the contents of their metapleural glands to disinfect the wounds of nestmates, and the most abundant protein in this social transfer has no orthology to any known protein, indicating a very young gene [145]. In addition to species-level comparisons, inspecting population-level variation [28] would allow testing population genetic models of genes with indirect fitness effects [146].

Overall, when socially transferred materials and their impacts are better known, it will become possible to analyze the fitness costs and benefits for both the donor and the receiver, or in some cases, for the whole social group. Understanding how costs and benefits vary over socio-ecological contexts and evolutionary time scales, and how the dynamics of cooperation and conflict shape the evolutionary trajectories, will help us understand the role of these transfers in the evolution of social behavior and physiology. Such studies are still rare or non-existent outside the flagship socially transferred materials of seminal fluid and milk, but give great promise for answering fundamental evolutionary questions. In future work, the physiological and ecological costs and benefits could possibly be manipulated to develop practical applications (Box 2).

BOX2: Potential applications

Socially transferred materials can be used to screen for diagnostic biomarkers for diseases and conditions. This has already proven to be useful for monitoring fetus development with amniotic fluid biomarkers [147,148] or seminal fluid in connection to fertility [22,149,150]. Outside human medicine, similar applications are equally useful in agriculture and food science, as shown by the vast literature of bovine milk biomarkers [151].

Secondary components of socially transferred materials can function outside the context and species where they originally evolved. Egg yolk low-density lipoproteins or milk casein micelles seem to protect sperm during preservation [152,153]. Royal jelly extends healthy aging and lifespan not only in honey bees but also in *D. melanogaster*, *C. elegans*, and *M. musculus* [154]. Because socially transferred components can be used across transfers and across taxa, secondary components may be used for future drug delivery given their functions in stabilization (e.g. RNA binding proteins [86]), or packaging and delivery (e.g. extra-cellular vesicles [155–157]). In addition to drugs, the delivery of probiotic bacteria [158,159] may benefit from the study of socially transferred materials, as many social transfers have evolved components to stabilize the transfer of symbionts across individuals. Recently, the SARS-CoV-2 pandemic has resulted in a renewed interest in the ability of maternal milk to transfer antibodies and other immune components [160].

The performance of socially transferred materials can potentially be enhanced by altering their composition. Studies on such approaches have mostly focused on single functional molecules. For example, the agricultural industry benefits from understanding which molecules affect seminal fluid in *in vitro* fertilization [161] and sperm cryopreservation [162,163], which could be equally beneficial in conservation [164] or human medicine. In addition to improving the biological materials themselves, the composition of artificial substitutes such as infant formula can be altered [165]. Understanding the context dependencies of natural milk could offer great improvements for more individually tailored formulas.

The above examples require mechanistic knowledge and proximate understanding of socially transferred materials. When this knowledge is placed in the evolutionary context, and especially when the underlying balance of benefits and costs is considered, different types of applications can be found. Understanding how sexual or parent-offspring conflict shapes the composition of eggs, sperm, seminal fluid or milk could help to push the conflict towards a desired outcome, for example in human fertility, animal breeding or research. Understanding how a social insect colony uses socially transferred materials to produce colony-level physiological outcomes [24] would allow targeted colony manipulation in pest ants and termites, and pollinating bees. Pest species can potentially be controlled also using knowledge about how their mating partners manipulate their reproductive physiology. Applications for biocontrol may be possible even across species (similarly to [166]).

Concluding Remarks

Socially transferred materials are an effective and taxonomically widespread means for one individual to impact another. The diverse molecular machineries of these materials show how evolution has brought about many fascinating solutions to direct and manipulate conspecifics, but also many commonalities across types of transfer and taxa. Several theoretical approaches can be used to study the evolution of these materials, and they also offer new ways to test old evolutionary theories. Here we outline necessary theoretical work to move this field forward and to answer the *Outstanding questions.*

Proximately, socially transferred materials can have very complex and dynamically changing compositions, often with ample functional redundancy. Previous studies on communication signals have shown similar evolutionary paths towards seemingly unnecessary complexity, and their insights are valuable for understanding socially transferred materials [167,168]. There are various theories on why such complexity evolves: to balance the costs and benefits of single signals, or their mixture as a whole, or to increase robustness and counter transmission difficulties with noisy signals or the physiological constraints in producing some of them. Additionally, there can be multiple messages delivered, by multiple donors to multiple receivers. It is also possible that some parts of the transferred material exist to eliminate cheaters (e.g. parasites or conspecific competitors) and so are the product of a completely different co-evolutionary interaction beyond the donor and direct receiver. Redundancy may exist to allow the maximum plasticity and robustness in different contexts, or as a legacy of past resistance in receivers. Overall, the history of research on animal signals highlights an important lesson: receivers likely have a role in shaping the components of socially transferred materials – just as they have in shaping communication signals.

Ultimately, costs and benefits for both donors and recipients drive the evolution of socially transferred materials. These can be measured as energy, but more comprehensively in terms of direct and indirect fitness [169,170]. Thus, the inclusive fitness framework of kin selection theory is useful to understand the parallel evolution of socially transferred materials across behavioral contexts, and helps in assessment of the inherent risks of opening a direct physiological channel between individuals. This framework best allows the formation of hypotheses for the kinds of materials that can evolve under different levels of conflict, and between more or less related individuals.

In theory, genes with social effects on fitness are expected to evolve more rapidly than genes that only influence an individual's own fitness [10,146,171]. Especially under strong conflicts and therefore high costs, there is selection for both conflict resolution and evolutionary arms races to lower costs, possibly accelerating evolution and adding to the complexity of these materials. However, the expectations for evolutionary rates of socially transferred materials are not straightforward, because negatively correlated indirect and direct genetic effects in the interacting partners may even reverse the expected evolutionary outcomes and slow the evolutionary rate [11]. Evolution under relaxed selection is also possible [144]. In light of these complications, considering indirect genetic effects in the game theory framework might allow prediction of evolutionary outcomes and create more easily testable hypotheses for empirical studies [172].

In some cases, the payoffs of material transfer depend not only on the interacting partners themselves, but on their previous interactions, making selection somewhat frequency dependent, and here the game theory approach may be especially fruitful. For example, female's fecundity can be stimulated by male's seminal fluid proteins at the first mating. Then, later mating males are selected to be sensitive to their position in the mating sequence [173,174], and to allocate resources accordingly, e.g. not investing in fecundity-stimulating proteins [174]. The same principle likely applies in other contexts, such as investment in defensive components [175]. Further, since socially transferred components can change an individual's physiology, they can influence that individual's subsequent social interactions, long after the donor has left the scene. For example, fecundity stimulation by one male can be seen as a service to its rivals, fundamentally changing the value of the resource that is being contested, altering the evolutionary pathways in line with fighting theory [176]. Contrastingly, in a simultaneous hermaphrodite, certain seminal fluid components lower the future fecundity of the mating partner in the male-role [177].

The above frameworks are ideal for explaining the derived adaptations in socially transferred materials and also their potentially large role in driving social evolution. With ecological and developmental feedback loops, these materials may provide positive feedback mechanisms and points of no return that create greater levels of cooperation, coordination and social control (e.g. evolution of group living from parental care [178–180], or the evolution of parental care and lactation in mammals (Figure 2)). In extreme cases, social transfers may evolve to integrate the physiology across individuals, even leading to group-level metabolism as in social insect colonies [35]. This suggests that social transfers may have been an important step toward the evolution of multicellularity. Inspecting socially transferred materials explicitly in the light of evolutionary theory will give us new insights into their proximate functions and into the ultimate role of social transfers as drivers of social evolution.

Outstanding Questions

- How much convergent evolution is there across socially transferred materials? Enough data already exist to conduct initial meta-analyses for a limited number of transfers, and more data should be generated to fill the gaps for other taxa and transfers.
- Where in gene regulatory networks do the underlying genes exist, in both the donor and the receiver, and what is their evolutionary age and rate of evolution? Are there genomic signatures of convergent molecular evolution?
- We hypothesize that the evolutionary route is from simple material transfers (genetic material/ nutrition/ symbionts) towards more complex transfers with increasing number of secondary components. This can be tested by comparing evolutionarily young transfers to older ones.
- According to kin selection theory, the levels of cooperation and conflict, and the relatedness between the partners, govern many aspects of social transfers, from rate of evolution to the transfer frequency. Establishing which transfers are more cooperative or competitive is an important future direction both theoretically and functionally, and allows further phylogenetic comparisons for the other aspects of these transfers.
- Analyzing the evolutionary routes and especially points of no return in socially transferred materials furthers our understanding on how costs and benefits can change, even from initially beneficial to highly costly, and how such runaway evolution and feedback loops create novel evolutionary directions.
- Understanding how the evolution of two-way transfers differs from unidirectional transfers offers an interesting viewpoint into the evolutionary constraints on social transfers. Reproductive transfers in hermaphrodites provide an excellent study system for these types of questions.
- Plasticity is an important aspect of socially transferred materials in both donors and receivers, likely linked to robustness and dynamic context-dependency. We hypothesize that the full mixture of components is ultimately more important than any single component.
- Although this review focuses on animal research, there are similar material transfers happening also in plants, fungi, and bacteria (conjugation, cross-feeding). Analyzing the taxon-specific and universal principles of these transfers will further our understanding of the evolutionary principles behind them.

Glossary

Allohormone: substances that are transferred from one individual to another (free-living) member of the same species and that induce a direct physiological response, bypassing sensory organs [15]
Primary component: the main material that a social transfer has evolved to transmit from donor to receiver: e.g. genetic material, nutrition or symbionts
Secondary component: molecular and cellular components of socially transferred materials that are not the primary cargo; allohormones, stabilizing or transport molecules, even functional cells
Social transfer (as used here): the behavior through which socially transferred materials are passed between individuals and which evolved for this purpose; e.g. lactation, copulation
Socially transferred material: materials transferred between conspecifics that i) include components metabolized by the donor, ii) which bring about a direct physiological response in the receiver, bypassing sensory organs, and iii) that benefit the donor.
Trophallaxis: direct ingestion by one individual of material excreted, secreted or regurgitated by another [5]
Vehicle: the combination of materials that evolved to allow socially transferred materials to be passed from one individual to another; e.g. egg, milk, ejaculate, mucus, specialized symbiont capsules etc.

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