Chromosome segregation during cell division in higher eukaryotes is driven by a microtubule spindle formed in the cytoplasm. To allow the interaction of microtubules and chromosomes, the nuclear envelope breaks down in prophase, leading to an 'open' mitosis. Nuclear envelope breakdown occurs by stepwise disassembly of nuclear pore complexes, inner nuclear membrane proteins and, finally, lamins, and is thought to be driven mostly by the phosphorylation of these proteins by mitotic kinases. In somatic cells, nuclear envelope breakdown is additionally facilitated by mitotic microtubules, which pull on the nuclear envelope creating invaginations which eventually cause rupturing of the stretched nuclear lamina. Nuclear membranes are absorbed by the ER, where nuclear membrane proteins disperse by diffusion. Interestingly, some nuclear envelope proteins appear to have additional functions in mitosis; for example, a subset of nucleoporins becomes part of the kinetochore complex that mediates microtubule–chromosome attachment and these nucleoporins are required for faithful chromosome segregation.

And how does the nuclear envelope reform? In species with an open mitosis, reformation of the nuclear envelope starts during anaphase and lasts into G1 phase of the cell cycle. Nuclear assembly is regulated both by the reversal of the mitotic phosphorylation of many nuclear envelope proteins and by the local action of Ran on chromosomes. The first proteins of the nuclear envelope known to bind to chromatin in anaphase are a subset of nucleoporins; these are followed by proteins of the inner nuclear membrane, which accumulate in ER membrane domains adjacent to anaphase chromatin, most likely by interacting with their binding partners on chromatin. Closure of these ER-derived membranes around chromatin and incorporation of nuclear pores requires membrane fusion events, the mechanism of which is still largely unknown. The nuclear lamina only reforms after the nuclear envelope has been sealed and functional nuclear pores import lamins into the nucleus.

Are there any diseases related to the nuclear envelope? Nuclear envelope proteins are implicated in many human diseases, though they tend to be very rare. Various nuclear envelope proteins are targets of autoantibodies in autoimmune diseases such as primary biliary cirrhosis. Defects in nucleocytoplasmic transport, altered expression of nuclear transport factors and chromosomal translocations of nucleoporins have all been implicated in certain types of human cancer. Mutations in the nucleoporin ALADIN cause triple A syndrome, a complex disease characterized by a particular combination of severe tissue specific defects. The largest disease group associated with the nuclear envelope are termed laminopathies, because they result from mutations mainly in the lamin A/C gene, but also in lamin interacting proteins like emerin or proteins involved in the biogenesis of mature lamin A. Although these proteins are ubiquitously expressed, the diseases exhibit diverse tissue specific symptoms ranging from myopathies and neuropathies to lipopathies and progeria syndromes (premature aging), depending on the specific mutation in the gene. The molecular mechanisms of these diseases are not yet understood; hypotheses range from failure to resist mechanical stress in muscle to aberrant regulation of gene expression.

Where can I find out more?

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Primer

Bees

Bryan Danforth

It is almost impossible to imagine a world without bees. Bees are an important component of virtually all terrestrial habitats and they are major pollinators of flowering plants (angiosperms), the predominant group of vascular plants, throughout the world. There are currently over 16,000 described species of bees (Michener 2000) and their evolutionary history extends well back to the early Cretaceous, a period of major angiosperm diversification. It is likely that bees and angiosperms co-radiated. That is, bee diversification may have facilitated angiosperm diversification and vice versa. Today bees perform a vital ecosystem function as the dominant pollinators of flowering plants in both natural and agricultural ecosystems.

Bees are important pollinators of many economically important crops, including apples, watermelon, pumpkins, squash, grapefruit, coffee, tomatoes and sunflowers. The economic and ecological impact of bees is immense. Honey bees alone are estimated to contribute $14 billion a year to the US economy and a recent study estimated that native bees (non-honeybees) contribute ~$3 billion in pollination services to the US economy each year. Bees are essentially specialized herbivores.They are unusual herbivores, however, because their effects on plants are not entirely negative — they are important and efficient pollinators (with a few exceptions) of many angiosperm plants and their impact as pollinators must greatly outweigh their negative impacts as herbivores.

Bees are also important social insects. Bees, especially the honey bee and related corbiculate bees, have served as models for understanding the dynamics within eusocial insect colonies. Remarkable, perhaps to many

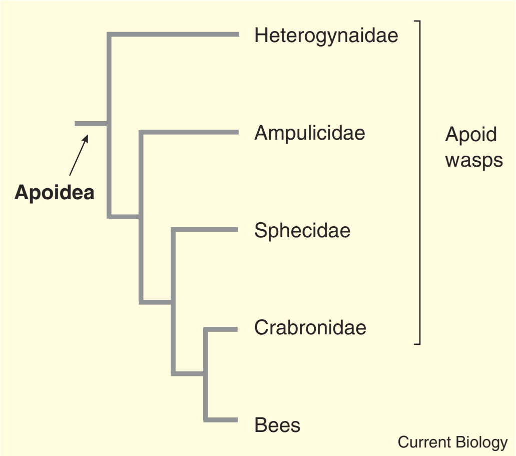

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Figure 1. Phylogenetic affinities of the extant lineages of Apoidea, including bees.

people, is that a relatively small proportion (~6%) of all bees are eusocial (showing reproductive division of labor, overlap of generations and cooperative brood care). The vast majority are solitary nesting species with a univoltine life-cycle.

Origin and evolutionary history

Bees are believed to have arisen approximately 100 to 120 million years ago (the Early Cretaceous). Bees are closely related to the predatory sand wasps, from which they are derived (Figure 1). While bees share many life history traits with sand wasps, they have evolved a number of novel morphological and behavioral traits. Among the most important is that bees are herbivores, feeding on pollen and nectar of angiosperm plants, whereas sand wasps are carnivores that feed their young insects and spiders as a source of protein. Morphological features unique to bees include their finely branched, plumose hairs and the expanded hind basitarsus (a segment of the hind leg) in females. These and other characteristics of bees are adaptations for collecting pollen rather than invertebrate prey. The monophyletic group including the wasp families Heterogynaidae, Ampulicidae, Sphecidae and Crabronidae, as well as bees, is referred to as the superfamily Apoidea (Figure 1).

Relationships among the major lineages (families and subfamilies) of bees remain controversial. Morphological studies (Alexander and Michener 1996) strongly support the monophyly of most families (except Colletidae and Melittidae), but fail clearly to resolve the relationships among families. While Colletidae is generally viewed as the most ‘primitive’ or basal lineage, this result is not strongly supported by morphological data, and some authors have expressed doubts about this interpretation. Recent molecular and combined morphological and molecular studies (Danforth *et al*. 2006) have supported a different view of higher-level bee phylogeny (Figure 2). According to this phylogeny, which is based on six genes, over 4000 base pairs of DNA sequence data and both parsimony and model-based methods, the root of the bees falls within Melittidae (*sensu lato*). This alternative topology essentially turns the status quo view upside down; Colletidae appears as a fairly derived lineage, for example. This tree topology has some important implications for understanding bee evolution. It implies that pollen-specialization, virtually universal within Melittidae, is a primitive trait for bees. It also suggests that early bee diversification may have occurred in Africa, where the majority of melittid diversity is concentrated. Finally, this tree topology corresponds more closely with the chronological appearance of bee fossils than the alternative (status quo) topology. It also helps explain the relative antiquity of eusociality in Apidae.

Figure 2. Phylogeny of the bee families.

The phylogeny shown is based on five nuclear genes – for proteins EF-1, LW rhodopsin and RNA polymerase II, and 18S and 28S rRNAs – plus morphology (Danforth *et al.* 2006). Values on the branches are bootstrap values with (above) and without (below) the morphological data. The tree was rooted with wasps from the families Sphecidae and Crabronidae.

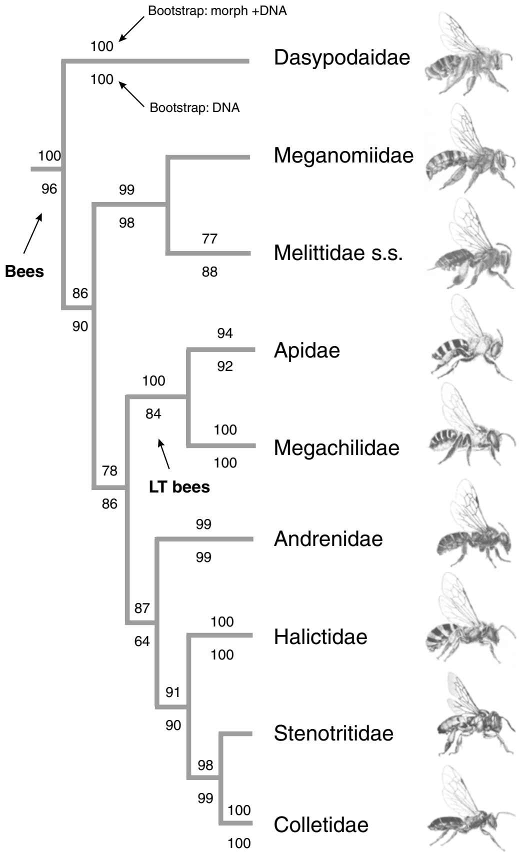

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Figure 3. Pollen balls.

The pollen balls in the photo were constructed by a female *Calliopsis* (*Hypomacrotera*) *persimilis*, an oligolectic (specialist) bee on Physalis (Solanaceae). Note the burrow (marked with white powder) to the right. (Photo credit: B.N. Danforth).

Much work remains to be done on bee phylogeny at all levels. With the availability of the honey bee genome sequence we have a virtually limitless choice of genes and gene regions from which to develop additional data sets. For many groups there is only a limited understanding of tribal and generic relationships, and for the vast majority of genera we do not have a clear understanding of species-level relationships.

Biogeography

Bees have their greatest diversity in arid and semiarid regions of the world, including Mediterranean climate regions, such as southern Europe, southern Africa, western Australia, arid parts of Chile and Argentina, and deserts of North America. These areas also tend to show high diversity and high levels of endemism in flowering plant species. The southern Hemisphere continents of Africa, South America, and Australia seem to host the majority of very ancient bee lineages, such as Melittidae, Fideliinae and Andreninae.

Some bee groups show evidence of South American/Australian interchange (via Antarctica). There are often striking differences in the bee fauna of different continents. Africa, for example, has a strikingly different bee fauna from South America, and Australia has a bee fauna dominated by one family (Colletidae). There are several examples of long-distance dispersal in bees, for example, *Hylaeus* in Hawaii, as well as disjunct distributions suggestive of great antiquity, such as *Hesperapis* (Melittidae *sensu lato*) in western North America and southern Africa.

Diversity and life history

While some bees are well known and important social insects, the majority of bee species are solitary. Six percent of all bee species are believed to be eusocial (described below). The vast majority of bees are either solitary nesting or cleptoparasitic on other solitary nesting hosts. A typical solitary bee, for example *Colletes*, *Dasypoda*, *Calliopsis* or *Anthophora*, normally exhibits a univoltine life-cycle. Females and typically, but not always, males overwinter or pass a relatively long unfavorable part of the year as last instar larvae. These larvae are quiescent and resistant to dessication and many species are believed to be able to remain in diapause for several years, like seeds. Pupation and emergence of adults is thought to be triggered by humidity or other environmental cues and females begin constructing nests shortly after emergence. Emergence of adults, at least in some species, is clearly tied to the period of host-plant flowering. This is especially true in arid and semi-arid environments, where flowers typically bloom for a very short period of time. Mating typically takes place on flowers or near the nestsite. Males in some species, for example *Anthidium*, are territorial, guarding floral resources valuable to females.

Female solitary bees are hard workers. A typical solitary female will provision one cell per day with from 2–20 pollen/nectar trips. Pollen is typically carried on the hind legs in a scopa located on the hind trochanter, femur or tibia, but some bees carry pollen on the undersurface of the abdomen or on specialized hairs on the lateral surface of the propodeum, or internally in the distensible crop. Small bees tend to make fewer trips per cell, possibly because of the allometric advantages of small body size. After her last foraging trip, the female sculpts the pollen loads into a ball or loaf by adding nectar stored in her digestive tract (Figure 3). Once the pollen mass is completed, the female typically lays just one egg and then closes the cell, with soil, mud, masticated wood or other material. Another cell is typically constructed overnight and provisioned the next day. This cycle continues for the life of the female.

There are many exceptions to this typical pattern. Some females may provision multiple (up to six) cells per day, and others may take multiple days to provision a cell. In *Parafidelia* (Megachilidae) females insert multiple eggs per pollen mass. In some solitary species females are known to perform a ‘feeding trip’ late in the day. During this ‘feeding trip’ females consume pollen and nectar for their own nutrition. Consumption of pollen by females is likely related to the protein requirements of egg-laying. While it is true that for most bees pollen is the major protein source, there are exceptions to this rule. Some stingless bees in the Neotropics are actually scavengers on vertebrate carcasses. This reversion to a carnivorous lifestyle is a very rare feature of just a few, highly derived, bees.

Much variation exists in the nesting substrate used by bees.

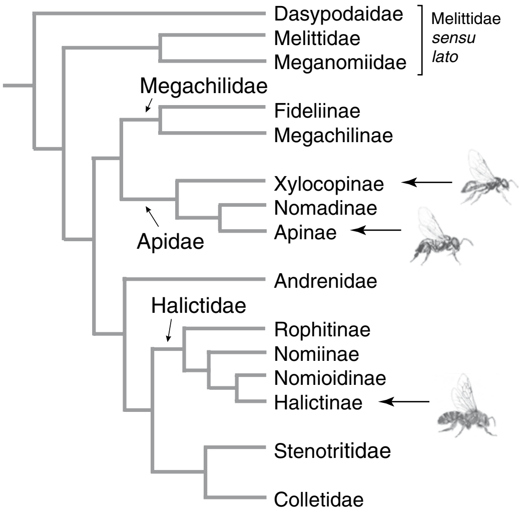

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Figure 4. Phylogeny of the bee families and subfamilies indicating the positions of the major eusocial lineages.

Xylocopinae, carpenter bees and relatives, including the eusocial and socially parasitic groups of Allodapini; Apinae, including the eusocial corbiculate tribes Bombini, Meliponini and Apini; Halictinae, including three origins of eusociality in Augochlorini, *Lasioglossum* and *Halictus*.

While many are ground-nesters which dig burrows in the soil, up to two meters deep in some species, there are also bees that build above-ground nests in stems or use pre-existing burrows, or make nests of mud (mason bees), resin or plant materials (carder bees); some (carpenter) bees excavate nests in wood.

While bees are normally thought of as diurnal organisms, some bees are crepuscular and some species are fully nocturnal. Crepuscular and nocturnal bees occur in several families, including Colletidae (Diphaglossinae), Halictidae, Andrenidae, and Apidae. True nocturnal foraging occurs in *Lasioglossum* subgenus *Sphecodogastra*, *Megalopta* (Halictidae), and the *Perdita* subgenus *Xerophasma* (Andrenidae). Both *Sphecodogastra* and *Xerophasma* are specialist foragers on evening primrose (*Oenothera*). In some species of *Sphecodogastra* females forage exclusively during moon-lit nights. Nocturnal foraging involves morphological adaptations including enlarged ocelli and compound eyes and pale coloration.

Among the most interesting, but poorly known, bees are the cleptoparasitic species. An estimated 20% of all bee species are cleptoparasites (cuckoo parasites) that lay their eggs in the nests of other bees. Cleptoparasitic bees are morphologically highly divergent from other bees. They are often heavily armored and lack pollen-collecting structures. Cleptoparasitic species are widespread in Apidae, Megachilidae, and Halictidae. There are only a few species of cleptoparasitic Colletidae (in the Hawaiian native bees in the subgenus *Nesoprosopis*) and no cleptoparasites have been reported from Melittidae, Andrenidae and Stenotritidae. Many cleptoparasitic groups have arisen from closely related (host) taxa but for most groups (Apidae and Megachilidae, in particular) phylogenies are too poorly resolved to be able to reconstruct the exact history of cleptoparasitism. Cleptoparasitism is estimated to have arisen over 25 times in bees.

Diversity in social behavior

While only 6% of bees are eusocial, there is enormous diversity among bees in social behavior. Some species form communal associations in which adult, reproductively active females share a common nest. There is no cooperation among females in provisioning but there may be advantages in collective nest defense. In more social species female nestmates show reproductive division of labor, with some individuals foraging and providing nest defense, while others lay the majority of eggs. When these females are of the same generation we call these societies *semisocial*. When they are of different generations we call them *eusocial*.

Eusociality has arisen multiple times just within the bees (Figure 4). Earlier estimates of the number of origins of eusociality in bees may have been overestimates because generic and subgeneric relationships within halictine bees were not well understood. We now believe that obligate eusociality has had a total of five origins in bees: once in the common ancestor of Bombini, Meliponini and Apini, once in the common ancestor of Allodapini, and three times in the halictid subfamily Halictinae. Eusocial colonies are enormously variable in size and complexity. Some eusocial halictid colonies consist of just one queen and fewer than five workers, while honey bee colonies may contain a single queen and over 100,000 workers. In some cases, eusocial lineages may reach a ‘point of no return’ in which the lineage can no longer revert to solitary nesting. This has apparently occurred in ants and corbiculate bees, but reversals from eusociality to solitary nesting appear to be common in at least two genera of halictid bees: *Halictus* and *Lasioglossum*.

The honey bee (*Apis mellifera*) has provided important insights into the dynamics of social insect colonies (Winston 1987), and the recent publication of the honey bee genome sequence paves the way to an understanding of the genetic basis of some important eusocial traits, such as caste polymorphism, age polyethism, and reproductive division of labor.

Eusocial complexity and antiquity appear to be loosely correlated in bees, supporting the view that the ‘point of no return’ may take many millions of years to reach. Eusociality in the corbiculate Apidae is at least 65 million years old because a stingless bee (*Cretotrigona prisca*, Meliponini) species has been recovered from New Jersey amber estimated to be that age. Allodapine eusociality extends back at least to the Eocene (42 million years before present), because allodapine fossils are known from Baltic amber. Eusociality in the Halictinae appears to be much more recent.

Figure 5. A *Macrotera* (*Macroteropsis*) *portalis* male emerging from closed flower of *Sphaeralcea*.

Females in this species are narrow specialists on this genus of Malvaceae in the south-western US. (Photo credit: B.N. Danforth.)

Three origins of eusociality in Halictinae are estimated to be approximately 20–22 million years old, making these some of the most recent origins of eusociality known in insects. Within the eusocial halictine bees there are several examples of 'secondarily solitary' species. Reversion from eusociality to solitary nesting is particularly common among halictine bees, presumably because eusociality evolved relatively recently in this group of bees.

In summary, bees provide one of the best models for understanding the evolutionary transitions between solitary and eusocial behavior. Ants, termites and paper wasps show fewer origins of eusociality, and eusociality is considerably older in these groups than in bees. The fact that bees show multiple origins of eusociality, and that these origins span a broad time period from the late Cretaceous to the Miocene, makes bees an ideal model system for understanding social origins and evolution.

Floral rewards and host–plant associations

The bees that are most familiar to people — honey bees, bumblebees, large carpenter bees — tend to have very broad host-plant preferences. Honey bees, for example, will collect pollen from over 100 families of plants and have even been reported to collect gynosperm pollen from the surfaces of automobiles. Many bees, however, show much more narrow host-plant preferences, and some bees may restrict their pollen collecting to just one species or a closely related group of host-plants. Such 'oligolectic' (specialist) bees are restricted phylogenetically such that tribes and subfamilies of bees can be loosely described as specialists. The Melittidae (*sensu lato*), Fideliinae (Megachilidae), Rophitinae (Halictidae), Panurginae and Andreninae (Andrenidae, Figure 5), Scrapterinae and Paracolletinae (Colletidae), and several tribes within Apidae (Eucerini and Emphorini, for example) all tend to include large proportions of specialist bee species. Specialization of many of these groups can involve both behavioral and morphological traits.

Few studies have analyzed the evolution of host-preference in bees, but those that have (for example, Sipes and Tepedino 2005) have found that host plant associations are phylogenetically constrained — they persist over time within monophyletic lineages of bees — but that host switching, when it occurs, seems to be unrelated to host-plant phylogeny and may be related to floral morphology or chemistry. Why certain bees specialize and others show more broad host-plant preferences has not been fully resolved. It does appear that specialization is most prevalent in arid and semi-arid regions. Some evidence points to the possibility that specialist bees are more prone to extinction as a result of anthropogenic habitat alteration.

The most common floral rewards for bees are nectar and pollen. From the perspective of most bees, pollen is the most important floral resource because pollen is what limits bee reproduction. Pollen is also the basis of much of bee host-plant preference. However, pollen and nectar are not the only floral rewards. Plants in eight orders – 10 families, 79 genera and more than 2400 species – are known to provide floral oils as pollinator attractants and a limited number of highly specialized bee genera and species have evolved morphological adaptations for extracting and manipulating these viscous and highly nutritious floral oils (Buchmann 1987). Oil-collecting bees, such as *Macropis*, *Rediviva*, *Ctenoplectra*, *Tetrapedia*, *Tapinotaspis* and *Centris*, are among the most highly specialized of all bees.

Floral scents and odors can also be an important attractant but in this case it is males (not females) who are attracted to these rewards. In orchid bees (Euglossini), for example, males collect waxy materials from orchids that are mixed in a highly modified hind-leg and used to attract females. Resins used in nest construction may serve as floral rewards for some megachilid (*Heriades*, and *Hypanthidium*) and apid (*Euglossa*, *Eulaema*, *Eufriesia* and *Trigona*) bees. Resins are obtained from some species of *Dalechampia* and *Clusia* in the neotropics (Armbruster 1984). There is at least one case — involving *Ophrys*, an orchid, and *Andrena*, a solitary bee — in which pollination occurs through deception on the part of the flower. Early in the flowering season *Ophrys* orchids emit odors that mimic the scent of receptive female *Andrena* and the floral morphology adds to the deception. Males find these flowers attractive and attempt to mate with them, transferring orchid pollinia in the process (Simpson and Neff 1981).

Like all herbivores, bees show a broad range of specialization. But what makes the bee–plant interactions so interesting is that plants benefit from bee visitation at the same time the bees benefit from floral reward exploitation. The congruent and sometimes conflicting interests of the plants and the bees has led to a fascinating and ancient evolutionary interaction that may explain to some extent the incredible diversity of angiosperms (and bees) on earth.

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Visual pigments of the platypus: A novel route to mammalian colour vision

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The ancestral complement of cone visual pigments in vertebrates comprises four classes whose protein components are encoded by opsin genes and whose spectral sensitivities range from ultraviolet to red. This complement has been retained throughout the radiations of teleosts, amphibians, reptiles and birds. However, eutherian mammals have lost the shortwave-sensitive-2 (*SWS2*) and middlewave-sensitive (*Rh2*) classes [1] and retain only the longwave-sensitive (*LWS*) and shortwave-sensitive-1 (*SWS1*) classes. Most eutherians are, therefore, dichromats, with red-green colour blindness, with the exception of primates in which full trichromacy has been reinstated through the duplication of the *LWS* gene [2]. We have now found that monotremes are also exceptional amongst mammals in retaining the *SWS2* class.

The oviparous monotremes diverged from the viviparous placental and marsupial mammals around 200 mya [3]. Extant monotremes are represented by a single species of platypus (*Ornithorhynchus anatinus*) (Figure 1B), and two genera of spiny ant-eaters or echidna, *Zaglossus* and *Tachyglossus*. Their distribution is restricted to Australia and New Guinea. Working with platypus genomic DNA, we have amplified exon 4 of the *SWS2* and *LWS* cone opsin genes, as well as the *Rh1* rod opsin gene (Supplemental data). Using these sequences to search the recently released sequence (v38) of the platypus genome (http://pre.ensembl.org/Ornithorhynchus_anatinus), we identified a number of contigs with high identity to these sequences: ultraContig 426 contains *SWS2* and *LWS* sequences and ultraContig 358 the *Rh1* sequence. Subsequently, we used individual exons from each of the five opsin gene classes (including the *SWS1* and *Rh2* cone opsin genes) from representative vertebrate species (green anole, zebra finch, fat-tailed dunnart and human) to search the platypus genome for complete gene sequences. With the exception of *SWS1* and *Rh2*, each exon highlighted the same contigs identified by the initial search with the platypus exon 4 gene fragments, thereby enabling the identification of full sequences for two of the cone opsin genes, *SWS2* (GenBank accession: EF050077) and *LWS* (GenBank accession: EF050078), as well as the *Rh1* rod opsin gene (GenBank accession: EF050076) (Figure 1A; Supplemental data).

By contrast, only exon 5 of *SWS1* could be found and is located on ultraContig 278 (Figure 1A). This contig also contains the syntenic genes *CALU* and *NAG6* that flank *SWS1* in other species, so this is probably the correct genomic location. A large unsequenced region is present upstream of this exon (Figure 1A), and it is possible that the remainder of the gene is present within this region. However, despite numerous attempts, we have been unable to amplify any of the remaining exons from genomic DNA, indicating that the remainder of *SWS1* has probably been deleted during evolution.

No genomic sequences corresponding to *Rh2* could be found. In chicken, the *Rh2* gene is flanked by *MLN* and *GRM4* and these genes remain syntenic in the human genome. Both genes map to contig 17694 of the platypus genome, separated by 699 kb of sequence of which only 5% is undetermined. No *Rh2* sequence is present in this contig and numerous attempts using degenerate primers failed to amplify *Rh2* gene fragments from platypus genomic DNA. It is,