Trends in Parasitology

CellPress REVIEWS

Opinion

Photoparasitism as an Intermediate State in the Evolution of Apicomplexan Parasites

Miroslav Oborník[1,2,*]

Despite the benefits of phototrophy, many algae have lost photosynthesis and have converted back to heterotrophy. Parasitism is a heterotrophic strategy, with apicomplexans being among the most devastating parasites for humans. The presence of a nonphotosynthetic plastid in apicomplexan parasites suggests their phototrophic ancestry. The discovery of related phototrophic chromerids has unlocked the possibility to study the transition between phototrophy and parasitism in the Apicomplexa. The chromerid *Chromera velia* can live as an intracellular parasite in coral larvae as well as a free-living phototroph, combining phototrophy and parasitism in what I call photoparasitism. Since early-branching apicomplexans live extracellularly, their evolution from an intracellular symbiont is unlikely. In this opinion article I discuss possible evolutionary trajectories from an extracellular photoparasite to an obligatory apicomplexan parasite.

Highlights

Apicomplexan parasites evolved from a phototrophic ancestor.

Parasitism evolved multiple times in the Apicomplexa and in Apicomplexa-like protists.

Chromerid algae are the closest known phototrophic relatives of parasitic Apicomplexa.

The chromerid *Chromera velia* is a free-living alga that can infect coral larvae and live like a parasite.

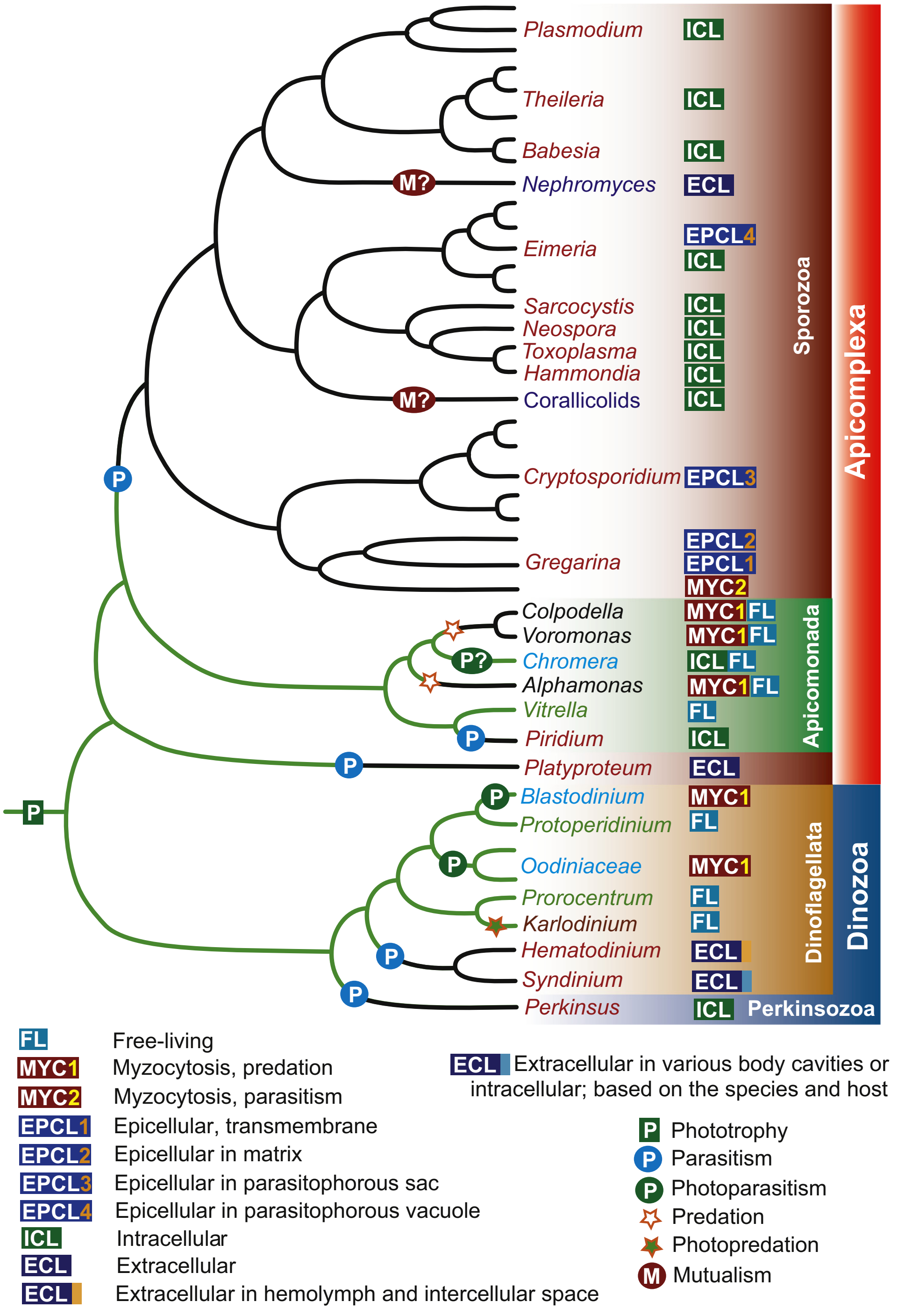
Apicomplexans Are Parasitic Algae

Apicomplexan parasites are obligate parasites of animals, including humans. They are responsible for hundreds of thousands of deaths annually (malaria) and high economic losses. These alveolate parasitic protists are characterized by the presence of the apical complex, a set of tubular and vesicular organelles at the anterior apex of the cell used for penetration of the host cell [1]. Apicomplexan parasites contain highly reduced organelles; the mitochondrion and the **apicoplast** (see Glossary), a relic nonphotosynthetic plastid [1,2]. The plastid has lost photosynthetic function, is surrounded by four membranes, suggesting its origin in a **complex endosymbiosis,** and contains a circular genome about 35 kb in size which lacks any traces of genes encoding photosynthetic functions [3–7]. Despite the absence of photosynthetic ability, the plastid is essential for the host cell because it is responsible for the synthesis of indispensable compounds such as heme, isoprenoids, and fatty acids. However, not all apicomplexans contain the plastid. Although complete loss of the plastid is quite rare in nature it has happened at least three times in the evolution of the **Apicomplexa** [3,4,8] (Figure 1): in protists of the genus *Cryptosporidium*, intestinal parasites of mammals and birds, and twice in neogregarines [8], a group of gregarines that usually infect the gut of insects and worms [1]. Both groups of protists are related and constitute early branches in the apicomplexan phylogenetic tree (Figure 1); in some taxonomic systems the genus *Cryptosporidium* is even classified within the frame of gregarines [9]. Apicomplexans are members of myzozoans [9], a group of protists capable of myzocytosis, a modified version of phagocytosis. The group also contains coral-associated complex algae named **chromerids** [10,11]; their relatives, colpodellids, predatory nonphotosynthetic marine flagellates (Figure 2); and **dinoflagellates** – marine and freshwater algae with complex plastids [12]. Colpodellids contain a plastid that lacks both a genome and photosynthetic ability [13], but which hosts the same essential pathways as the apicoplast. The presence of the plastid in the Apicomplexa has led to the suggestion that these deadly parasites have evolved from a photosynthetic algal ancestor [2] and that they

[1] Institute of Parasitology, Biology Centre, Czech Academy of Sciences, Branišovská 31, 37005 České Budějovice, Czech Republic
[2] Faculty of Science, University of South Bohemia, Branišovská 31, 37005 České Budějovice, Czech Republic

*Correspondence:
obornik@paru.cas.cz (M. Oborník).

https://doi.org/10.1016/j.pt.2020.06.002



Trends in Parasitology

Figure 1. Phylogenetic Distribution of Different Types of Organism-Environment Interactions in Myzoza (Classification According to [9]). The group includes phototrophic free-living organisms as well as predators and parasites, with these trophic modes combined in photopredation and photoparasitism.

Glossary

Apicomplexa: a group of alveolate protists containing obligate parasites of animals, including humans. They include, for example, the causative agents of malaria (*Plasmodium* spp.), babesiosis (*Babesia* spp.), toxoplasmosis (*Toxoplasma gondii*), and cryptosporidiosis (*Cryptosporidium* spp.).

Apicoplast: the nonphotosynthetic relic plastid present in most apicomplexans. It is surrounded by four membranes, suggesting its origin in a complex endosymbiotic event, and it hosts metabolic pathways that are essential for parasite survival. The presence of the plastid suggests phototrophic ancestry of these parasites. Accumulating evidence shows that the apicoplast originated in a rhodophyte (or rhodophyte-derived) endosymbiont.

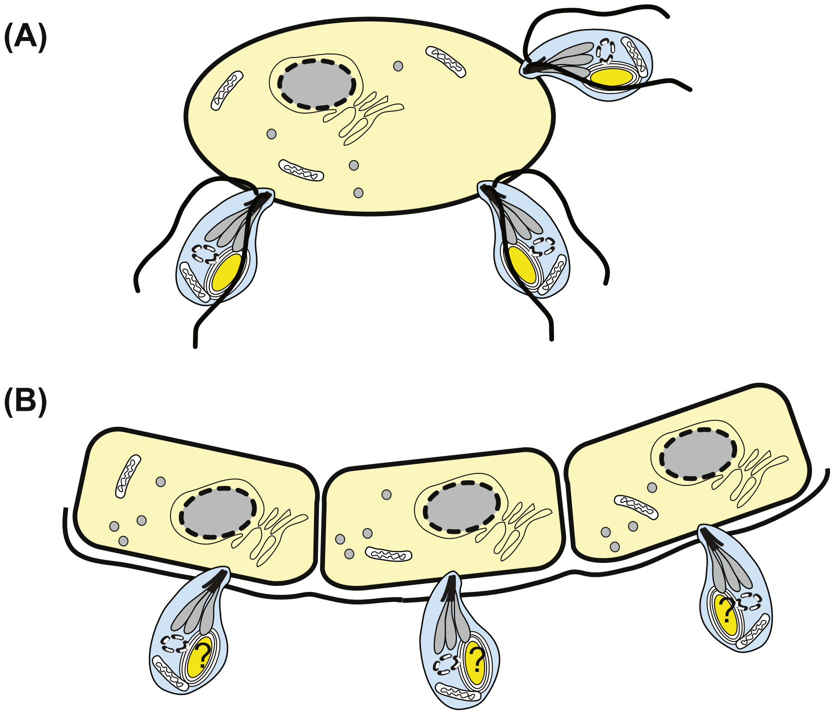
Chromerids: a group of algae closely related (together with the nonphotosynthetic predatory colpodellids) to the parasitic Apicomplexa. They contain a fully photosynthetic plastid, surrounded by four membranes, that lacks chlorophyll *c*, which is usually found in rhodophyte-derived complex plastids.

Complex endosymbioses: eukaryotic algae outside the Archaeplastida – such as stramenopiles (e.g., diatoms, eustigmatophytes, chrysophytes), alveolates (dinoflagellates, chromerids, and apicomplexans), rhizarians (chlorarachniophytes), haptophytes, cryptophytes, and euglenophytes – contain plastids surrounded by more than two membranes, usually three or four. Such plastid organelles originate in secondary, tertiary, or higher order eukaryote-to-eukaryote endosymbiotic events, involving a eukaryotic host and various eukaryotic algal endosymbionts with a primary or higher order plastid (chlorophytes, rhodophytes, stramenopiles, haptophytes, cryptophytes). Given the ongoing intense debate about the specific origin of plastids in secondary or higher order endosymbioses, I prefer the term 'complex endosymbiosis' (complex plastid).

Dinoflagellates: marine and freshwater algae with a complex plastid; they constitute a sister group to the Apicomplexa. Dinoflagellates are known to display a high diversity of plastids originating in complex endosymbioses (such as secondary and tertiary endosymbioses), plastid replacements, serial endosymbioses, or even loss of the plastid. Various dinoflagellates can live as phototrophs, mixotrophs, heterotrophs, or parasites.

Mixotrophy: a trophic mode combining phototrophy and various types of heterotrophy.

Photoparasitism: a mixotrophic lifestyle combining phototrophy and parasitism.



Trends in Parasitology

Figure 2. Co-occurrence of Predation and Parasitism. Colpodellids (A) are predators of algae and protists. They penetrate the cell surface to access the cytosol of the predated cell. The mode of action is, in principle, quite similar to that of early-branching apicomplexan parasites such as gregarines (B) living in the gut of various animals.

are just modified algae. However, the evolutionary pathway leading from a photoautotrophic alga to an obligate parasite had been, for a long time, difficult to trace because of the absence of close phototrophic relatives to parasitic apicomplexans. This obstacle was overcome by the discovery of chromerids [10,11].

Chromerids Are the Old Phototrophic Sisters of Parasitic Apicomplexans

Although the phototrophic ancestry of apicomplexans is beyond reasonable doubt, it was rather difficult to find their close photosynthetic relatives. The apicomplexan sister group, dinoflagellates, could not be efficiently used for meaningful comparison because they are too divergent. Frankly speaking, dinoflagellates are so unusual that they are difficult to compare to any other alveolates. They contain extremely large genomes, organized on chromosomes condensed during the entire life cycle, but are known to lack regular eukaryotic histones, which have been replaced by the virus-originated histone-like proteins [14]. Their original peridinin-pigmented plastid of supposedly secondary origin contains a highly reduced and diverse genome, containing only photosynthesis-related genes and ribosomal RNA genes, all located on minicircles [15]. Any attempts at comparison of the dinoflagellate plastid genome with that of the apicoplast failed, either because of no overlap in the protein-coding genes [16], or due to the high divergence of the rRNA genes [17,18]. Only the discovery of coral-associated chromerid algae [10,11] yielded a model useful for the comparison of relatively closely related phototrophic and obligate parasitic protists. So far, only two chromerid species, *Chromera velia* [10] and *Vitrella brassicaformis* [11], have been formally described and are available in culture. They are fully phototrophic, with plastid characterized by the absence of chlorophyll *c*, a pigment typical for algae with a rhodophyte-derived plastid [10,11]. Although the two species are the closest phototrophic relatives within apicomonads [9], they differ substantially in their morphology [10,11,19–23]; life cycles [10,11,21,23]; nuclear [24], plastid [25], and mitochondrial genomes [26]; and likely also their lifestyles. While an apical complex reduced to the form of the pre-conoid was found in *C. velia* [21,22], any such structure is absent from *V. brassicaformis* [23]. This may suggest a more intimate association between *C. velia* and its coral host than the second chromerid has.

C. velia – Mutualist, Epibiont, or Parasite?

Since *C. velia* was isolated from stony corals by a procedure usually used to isolate intracellular symbionts, it was initially assumed that the alga lives as a mutualist in coral, like the dinoflagellates of the genus *Symbiodinium* [10,27]. Nevertheless, attempts to detect *C. velia in situ* in an adult coral have so far failed; instead, the alga has been found only on the reef surface [28,29] and in coral-inferred environmental samples [30]. However, Cumbo and coworkers [31] have shown the presence of *C. velia* inside the ectoderm and endoderm of coral larvae in an unspecified symbiotic relationship, and this was followed by successful experimental infections. It was also shown that the alga invades the coral tissue within 24–42 h: some larvae die, but in others, the number of *C. velia* cells decreases within a week and the symbiont can even be completely eliminated. It follows that *C. velia* does not form a stable symbiotic relationship with corals. Disappearance of the temporary symbiont may suggest that it is either digested by the host cells or evicted from them. An experimental infection of *Acropora digitifera* by *C. velia*, followed by analysis of the transcriptomes of infected larvae, showed that they did not display a transcriptomic profile typical for any mutualistic association as it is known from the symbiotic dinoflagellates, but more likely resembles the transcriptomic profile of coral larvae infected by pathogenic bacteria. Since the immunity of the corals was significantly affected by the *C. velia* infection, and the endocytic pathway was reduced as well [32], it is very likely that *C. velia* can, under specific conditions, live as a facultative or accidental parasite of coral larvae [4,32]. It is likely that the type of *Chromera*–coral association highly depends on the protist strain used, the genotype of the infected coral, and the environmental conditions because, in some experiments, coral larvae can tolerate *C. velia* without any harmful effect [33]. However, the possibility that the absence of *C. velia* in adult corals is caused by the inability of infected larvae to establish a new coral colony cannot be rejected [4].

The accumulating evidence suggests that *C. velia* can live in a symbiotic, very likely parasitic, association with coral larvae [31–33]. At the same time, the alga is available in culture as a full phototroph [10], using highly efficient photosynthesis [34], despite the drastic reduction of photosystem subunits [35]. Moreover, there is experimental evidence suggesting that *C. velia* can live mixotrophically, combining phototrophy with the acquisition of simple organic molecules such as amino acids and sugars from the cultivation medium [36]. The **mixotrophy** of *C. velia* can thus comprise not only a combination of phototrophy and (supposed) osmotrophy, but also phototrophy and parasitism (see Outstanding Questions). This phenomenon, which I will call **photoparasitism**, is enabled by the translucence of the host coral larvae, allowing the alga to photosynthesize, to colonize the coral cells, and to obtain nutrients from its cytoplasm, all at the same time. Although photoparasitism is quite common in terrestrial parasitic plants [37] it is a very rare strategy for single-celled algae. Although there are many mixotrophs in the related dinoflagellates they mostly combine phototrophy and predation. There are several photoparasitic species known in rhodophytes [38], and a few dinoflagellates display such a lifestyle: for example, photoparasitic dinoflagellates of the genera *Oodinium*, *Amyloodinium*, and *Piscinoodinum* are ectoparasites of fish [39]. Similar to plants, ectoparasitism of dinoflagellates does not prevent photosynthesis because the parasite is exposed to light. Members of the genus *Blastodinium* –

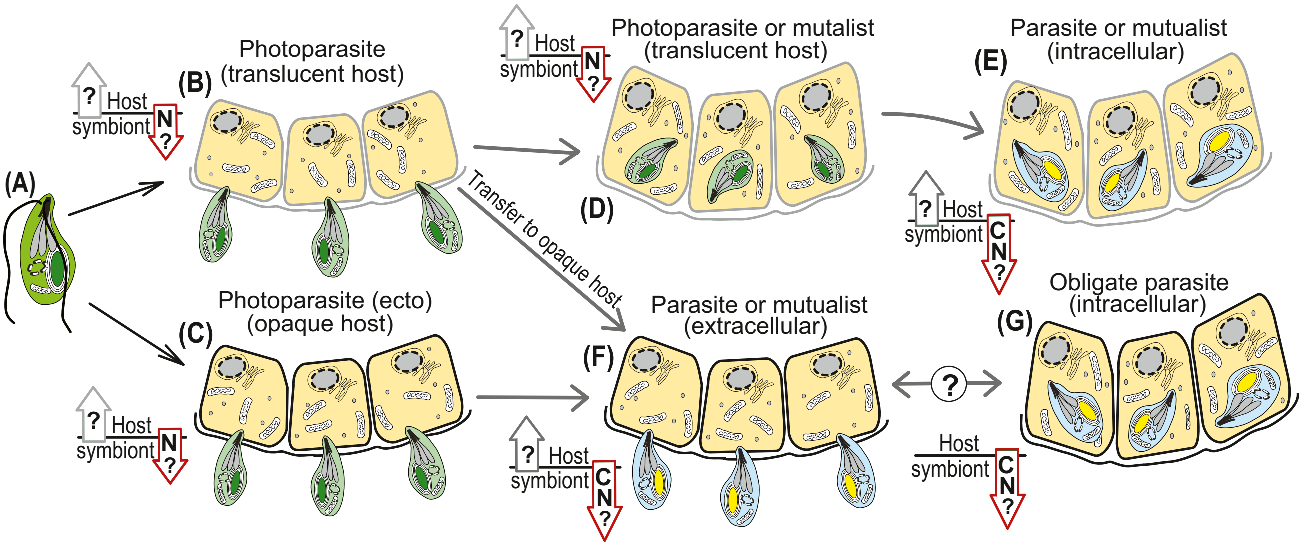
B. contortum, *B. navicula*, *B. galatheanum* – are unique because they live in the guts of the small marine copepods, *Clausocalanus arcuicornis, Corycaeus giesbrechti*, and *Acartia negligens*, respectively [40]. Again, due to the translucence of their hosts, they are likely capable of photosynthesis, although their photosynthetic activity is probably reduced [40]. This is, at least by one point, different from some mixotrophic (photopredatory) dinoflagellates (such as for example, *Karlodinium armiger*) which are known to increase photosynthesis after the ingestion of prey, especially when the prey is caught after a nitrogen starvation period [41]. In contrast, other dinoflagellates (e.g., *Fragilidium subglobosum*) decrease photosynthesis when they are living mixotrophically and have access to another source of organic carbon [42]. Consequently, it has been proposed that the photopredatory dinoflagellates and carnivorous plants likely do not hunt for their prey because of the need for organic carbon; rather, they are driven by the need for nitrogen and other essential elements [43]. I expect there to be a similar need for nutrients occurring in the photoparasitic protists.

Evolution of Obligate Parasitism in the Apicomplexa

The initial hypothesis concerning the evolution of apicomplexan parasites, proposing the evolution of parasites from a symbiotic (mutualistic) ancestor [27], was based on the presumption that *C. velia* is an intracellular phototrophic mutualist. Moreover, it assumed an evolutionary transition from a phototrophic mutualistic intracellular symbiont to an obligate apicomplexan parasite [27]. However, the contrast between supposed harmless, perhaps even mutualistic, apicomplexan endosymbionts, such as *Nepromyces* [44] and corallicolids [30], living in association with evolutionarily old marine hosts (sea grapes and corals) and the devastating apicomplexan parasites (*Plasmodium* and *Toxoplasma*) of evolutionarily young mammals, more likely suggests a different evolutionary trajectory. Corallicolids, heterotrophic intracellular coral symbionts harboring a complex nonphotosynthetic relic plastid similar to the apicoplast, are a particularly impressive case. Surprisingly, their plastid genome also contains, in addition to the housekeeping genes, four genes (*acsF*, *chlB*, *chlL*, *chlN*) normally utilized in the chlorophyll biosynthesis pathway. The function of these genes remains unknown because corallicolids, as heterotrophs, do not contain chlorophyll and are not able to synthesize it [30]. The eventual evolution of a harmless symbiont from a parasitic ancestor may reflect a long-standing host–symbiont adaptation or it could be the result of coinfection of the host with another symbiont [45], which can lead to less damaging pathogens and the maintenance of mutualisms [46]. It has been shown that both previously mentioned apicomplexan mutualistic endosymbionts, *Nephromyces* and corallicolids, live in multisymbiont systems [30,44,45] which can contribute to the evolution of harmless or mutualistic symbioses. The case of corallicolids [47] may indicate that photosynthesis could be retained in core apicomplexans (Sporozoa) longer than we thought, even in the intracellular stages. However, in my opinion, the photosynthesis genes in the plastid genome of corallicolids acquired a novel function which became beneficial for the coral hosts.

Recent discoveries demonstrate that obligate parasitism evolved from phototrophic ancestors several times independently in myzozoans [8,47,48] (Figure 1): in dinoflagellates, *Platyproteum* [47,49], *Piridium sociabile* [47,48], and apicomplexan parasites [1,9] (Sporozoa, according to Cavalier-Smith [9]). The apicomplexan *Platyproteum* sp. is formally classified as a gregarine [49]; however, the phylogenetic position of this extracellular parasite [47,48] is early branching, specifically at the root of all the Apicomplexa, including Apicomonada (Figure 1). In contrast to most other gregarines, *Platyproteum* seems to have a relic plastid [47]. Since it was previously included in the gregarine genus *Selenidium*, it is not without interest that a multimembrane vesicle resembling a relic plastid was referred to in *S. hollandei* by Schrével 50 years ago [50]. Losses of the plastid in apicomplexans have certainly been more common than previously thought. Loss of the plastid organelle, which is generally quite rare in nature, can be associated with limited plastid metabolism in the related photosynthetic chromerids, which, for example, lack plastid synthesis of most amino acids [51]. Although *P. sociabile* had been originally classified as a true apicomplexan parasite of marine mollusks [52] it more recently appears to be related to the chromerid *V. brassicafomis* [47]. The plastid genome of this parasite is quite similar to that in its phototrophic relative, lacking just a few genes coding for ribosomal proteins and three ORFs, together with missing photosynthesis-related genes. In addition to this, the *P. sociabile* plastid genome possesses ribosomal RNA genes arranged in tandem repeats (not inverted as in *Vitrella*), with one repeat drastically reduced to the 23S remnant [47,48]. Accumulating evidence [8,47] suggests that parasitism evolved multiple times in Apicomonada. Since corallicolids still contain photosynthesis genes in their plastids [30], I cannot rule out a similar scenario having occurred in the core apicomplexan parasites (Sporozoa).

However, despite the existence of *P. sociabile*, the Apicomplexa-like intracellular parasite [44,45], it is, in my opinion, likely that the core apicomplexan parasites (gregarines, haemosporidians, and coccidians) have not evolved from an intracellular *Chromera*-like ancestor because some early-branching parasitic gregarines and cryptosporidians are not intracellular (see Figures 1 and 3 for details). Parasites of the genus *Cryptosporidium* are epicellular: their cell is, when attached to the gut epithelium, gradually surrounded by the host cell, but they, in fact, never invade the host cell [53]. Other apicomplexan parasites have modified this mechanism by varying degrees. Even if they live intracellularly, most of them (exceptions are *Babesia* and *Theileria*) are surrounded by the parasitophorous vacuole [1]. An intracellular phase is, in general, found in neogregarines. In



Trends in Parasitology

Figure 3. Various Scenarios of the Evolution of Parasites in the Myzozoa. All the evolutionary pathways are understood to begin from a photosynthetic ancestor harboring a complex plastid (A). The initial interaction is supposed to be extracellular in a translucent host (B) or an opaque host (C). It can evolve to the interaction that is assumed for *C. velia*: the phototrophic alga is an intracellular symbiont (D) in a translucent host (coral). Such a symbiont can either be a mutualist, providing organic carbon to the host, or a photoparasite, living off a combination of photosynthesis and parasitic acquisition of nitrogen compounds. Such an organism can eventually evolve into a nonphotosynthetic symbiont (E) by losing photosynthesis (likely thanks to the acquired ability for the uptake of organic carbon from the host) or intracellular parasite (E). I propose that the ancestor of parasitic apicomplexans (Sporozoa according to [9]) was a photoparasite living extracellularly; it was either an ectoparasite (C) (lifestyle similar to dinoflagellates of the family Oodiniaceae), which lost photosynthesis (F) and became an intracellular obligate parasite through evolution (G), or more likely an intestinal photoparasite infecting a translucent host (B) (lifestyle similar to *Blastodinium*) that lost photosynthesis (F) likely due to infection of an opaque host and its loss of access to light, which subsequently became an intracellular parasite through evolution (G). The arrows show the proposed direction of the flow of carbon (C) and nitrogen (N).

most eugregarines and archigregarines such stages have not been found, but they have been referred to, for example, in the archigregarine *Selenidium pygospionis* [54]. I propose a novel pathway for the evolution of the apicomplexan parasites that initiated from a photoparasitic, rather than a mutualistic, ancestor (Figure 3). Furthermore, such a hypothetical organism was very likely not an intracellular symbiont like *C. velia*; being extracellular, in lifestyle, it more likely resembled parasitic dinoflagellates of the genus *Blastodinium* (Figure 3) [40].

The multiple origins of parasitism in the group may suggest a predisposition of myzozoans and myzocytosis for the parasitic lifestyle and their extremely high trophic plasticity. Conceptualizing the evolution of obligatory nonphotosynthetic parasites from a photoparasitic stage provides a trophic bridge for a continuous transition from photoautotroph to the fully heterotrophic parasite. In other words, the phototrophic apicomplexan ancestor developed parasitic capabilities first, and only then lost the ability of photosynthesis. Such a strategy makes the trophic transition much easier and does not exclude photoautotrophy, which we see in the chromerid, *C. velia*, as well as in photoparasitic dinoflagellates.

Concluding Remarks

Apicomplexan parasites are modified nonphotosynthetic algae, with coral-associated chromerids being their closest known phototrophic relatives [3–6,10,11,13,19,24]. The chromerid *C. velia* can live as a phototrophic free-living alga as well as an intracellular symbiont, likely as a facultative or accidental parasite of coral larvae [4,32]. Therefore, the alga lives mixotrophically, combining phototrophy and parasitism in a form called photoparasitism. Since early branching parasitic apicomplexans, the gregarines or *Cryptosporidium*, do not enter the host cell, unlike the advanced Apicomplexa (*Plasmodium*, *Toxoplasma*) [1], apicomplexan parasites have very likely not evolved from a *Chromera*-like intracellular ancestor. Rather, these parasites have evolved from an extracellular photoparasite resembling in its lifestyle dinoflagellates of the genus *Blastodinium*, which parasitize the guts of translucent marine copepods (see Outstanding Questions).

Outstanding Questions

Can photosynthetic chromerids live mixotrophically?

What is photoparasitism?

Do photoparasites need access to light?

Did apicomplexan parasites evolve from a photoparasitic ancestor?

Is *Chromera velia* a photoparasite?

Was an ancestor of apicomplexan parasites an intracellular symbiont?

Can mixotrophic dinoflagellates live as photoparasites?

Which photoparasitic dinoflagellate lifestyle resembles that of early apicomplexans?

Acknowledgments

I thank Julius Lukeš for the critical reading of this manuscript. I cordially thank Ross Waller, D. Wayne Coats, and Andrea Bardůnek Valigurová for helpful discussions, and Rachel Kolísko for language editing of the manuscript. I also thank the anonymous reviewer for their inspiring thoughts.

This work was supported by the Czech Science Foundation (18-13458S) and the ERDF/ESF Centre for research of pathogenicity and virulence of parasites (No.CZ.02.1.01/0.0/0.0/16_019/0000759).

References

1. Votýpka, J. *et al.* (2017) Apicomplexa. In *Handbook of Protists* (Archibald, J.M. *et al.*, eds), pp. 567–624, Springer
2. McFadden, G.I. *et al.* (1996) Plastid in human parasites. *Nature* 381, 482
3. Oborník, M. (2018) The birth of red complex plastids: one, three, or four times? *Trends Parasitol.* 34, 923–925
4. Oborník, M. (2019) Endosymbiotic evolution of algae, secondary heterotrophy and parasitism. *Biomolecules* 9, 266
5. Keeling, P.J. (2013) The number, speed, and impact of plastid endosymbioses in eukaryotic evolution. *Annu. Rev. Plant Biol.* 64, 583–607
6. Füssy, Z. and Oborník, M. (2018) Complex endosymbioses I: from primary to complex plastids, multiple independent events. In *Plastids: Methods and Protocols Methods in Molecular Biology* (vol. 1829) (Maréchal, E., ed.), pp. 17–35, Humana Press
7. Maréchal, E. and Cesbron-Delauw, M.F. (2001) The apicoplast: a new member of the plastid family. *Trends Plant Sci.* 6, 200–205
8. Janouškovec, J. *et al.* (2019) Apicomplexan-like parasites are polyphyletic and widely but selectively dependent on cryptic plastid organelles. *eLife* 8, e49662
9. Cavalier-Smith, T. (2018) Kingdom Chromista and its eight phyla: a new synthesis emphasising periplastid protein targeting, cyto-skeletal and periplastid evolution, and ancient divergences. *Protoplasma* 255, 297–357
10. Moore, R.B. *et al.* (2008) A photosynthetic alveolate closely related to apicomplexan parasites. *Nature* 451, 959–963
11. Oborník, M. *et al.* (2012) Morphology, ultrastructure and life cycle of *Vitrella brassicaformis* n. sp., n. gen., a novel chromerid from the Great Barrier Reef. *Protist* 163, 306–323
12. Waller, R.F. and Kořený, L. (2017) Plastid complexity on dinogflagellates: A picture of gains, losses, replacements and revisions. *Adv. Bot. Res.* 84, 105–143
13. Janouškovec, J. *et al.* (2015) Factors mediating plastid dependency and the origins of parasitism in apicomplexans and their close relatives. *Proc. Natl. Acad. Sci. U. S. A.* 112, 10200–10207
14. Irwin, N.A.T. *et al.* (2018) Viral proteins as a potential driver of histone depletion in dinoflagellates. *Nat. Commun.* 9, 1535
15. Zhang, Z. *et al.* (1999) Single gene circles in dinoflagellate chloroplast genomes. *Nature* 400, 155–159
16. Keeling, P.J. (2008) Bridge over troublesome plastids. *Nature* 451, 896–897

17. Zhang, Z.D. *et al.* (2000) Phylogeny of ultra-rabidly evolving dinoflagellate chloroplast genes: a possible common origin for sporozoan and dinoflagellate plastid. *J. Mol. Evol.* 51, 26–40
18. Oborník, M. *et al.* (2002) Phylogenetic analyses suggest lateral gene transfer from the mitochondrion to the apicoplast. *Gene* 285, 109–118
19. Füssy, Z. and Oborník, M. (2017) Chromerids and their plastids. *Adv. Bot. Res.* 84, 187–218
20. Oborník, M. *et al.* (2009) Evolution of the apicoplast and its host: from heterotrophy to autotrophy and back again. *Int. J. Parasitol.* 39, 1–12
21. Oborník, M. *et al.* (2011) Morphology and ultrastructure of multiple life cycle stages of the photosynthetic relative of Apicomplexa, *Chromera velia*. *Protist* 162, 115–130
22. Portman, N. and Šlapeta, J. (2014) The flagellar contribution to the apical complex: a new tool for the eukaryotic Swiss Army Knife? *Trends Parasitol.* 30, 58–64
23. Füssy, Z. *et al.* (2017) Budding of the alveolate alga *Vitrella brassicaformis* resembles sexual and asexual processes in apicomplexan parasites. *Protist* 168, 80–91
24. Woo, Y. *et al.* (2015) Chromerid genomes reveal the evolutionary path from photosynthetic algae to obligate intracellular parasites. *eLife* 4, e06974
25. Janouškovec, J. *et al.* (2010) A common red algal origin of the apicomplexan, dinoflagellate, and heterokont plastids. *Proc. Natl. Acad. Sci. U. S. A.* 107, 10949–10954
26. Flegontov, P. *et al.* (2015) Divergent mitochondrial respiratory chains in phototrophic relatives of apicomplexan parasites. *Mol. Biol. Evol.* 32, 1115–1131
27. Okamoto, N. and McFadden, G.I. (2008) The mother of all parasites. *Future Microbiol.* 3, 391–395
28. Janouškovec, J. *et al.* (2013) Environmental distribution of coral-associated relatives of apicomplexan parasites. *ISME J.* 7, 444–447
29. Mathur, V. *et al.* (2018) Global diversity and distribution of close relatives of apicomplexan parasites. *Environ. Microbiol.* 20, 2824–2833
30. Kwong, W.K. *et al.* (2019) A widespread coral-infecting apicomplexan with chlorophyll biosynthesis genes. *Nature* 568, 103–107
31. Cumbo, V.R. *et al.* (2013) *Chromera velia* is endosymbiotic in larvae of the reef corals *Acropora digitifera* and *A. tenuis*. *Protist* 164, 237–244
32. Mohamed, A.R. *et al.* (2018) Deciphering the nature of the coral–*Chromera* association. *ISME J.* 12, 776–790
33. Chakravarti, L.J. *et al.* (2019) Thermal and herbicide tolerances of chromerid algae and their ability to form a symbiosis with corals. *Front. Microbiol.* 10, 173
34. Quigg, A. *et al.* (2012) Photosynthesis in *Chromera velia* represents a simple system with high efficiency. *PLoS One* 7, e47036
35. Sobotka, R. *et al.* (2017) Extensive gain and loss of photosystem I subunits in chromerid algae, photosynthetic relatives of apicomplexans. *Sci. Rep.* 7, 13214
36. Foster, C. *et al.* (2014) Increased growth and pigment content of *Chromera velia* in mixotrophic culture. *FEMS Microbiol. Ecol.* 88, 121–128
37. Těšitel, J. (2017) Functional biology of parasitic plants: a review. *Plant. Ecol. Evol.* 149, 5–20
38. Blouin, N.A. and Lane, C.E. (2016) Red algae provide fertile ground for exploring parasite evolution. *Persp. Phycol.* 3, 11–19
39. Goméz, F. and Skovgaard, A. (2015) The molecular phylogeny of the type-species of *Oodinium* Chatton, 1912 (Dinoflagellata: Oodiniaceae), a highly divergent parasitic dinoflagellate with non-dinokaryotic characters. *Syst. Parasitol.* 90, 125–135
40. Skovgaard, A. *et al.* (2012) The parasitic dinoflagellates *Blastodinium* spp. inhabiting the gut of marine, plaktonic copepods: Morphology, ecology, and unrecognized species diversity. *Front. Microbiol.* 3, 305
41. Berge, T. and Hansen, P.J. (2016) Role of chloroplast in the predatory dinoflagellate *Karlodinium armiger*. *Mar. Ecol. Prog. Ser.* 549, 41–54
42. Hansen, P.J. *et al.* (2000) Physiology of the mixotrophic dinoflagellate *Fragilidium subglobosum*. II. Effects of time scale and prey concentration on photosynthetic performance. *Mar. Ecol. Prog. Ser.* 201, 137–146
43. Dagenias-Bellefeuille, S. and Morse, D. (2013) Putting the N in dinoflagellates. *Front. Microbiol.* 4, 369
44. Saffo, M.B. *et al.* (2010) *Nephromyces*, a beneficial apicomplexan symbiont in marine animals. *Proc. Natl. Acad. Sci. U. S. A.* 107, 16190–16195
45. Richards, T.A. and McCutcheon, J.P. (2019) Coral symbiosis is a three-player game. *Nature* 568, 41–42
46. Nelson, P.G. and May, G. (2020) Defensive symbiosis and the evolution of virulence. *Am. Nat.* (in press)
47. Mathur, V. *et al.* (2019) Multiple independent origins of apicomplexan-like parasites. *Curr. Biol.* 29, 2936–2941
48. Salomaki, E.D. and Kolisko, M. (2019) There is treasure everywhere: reductive plastid evolution in Apicomplexa in light of their close relatives. *Biomolecules* 9, 378
49. Rueckert, S. and Leander, B. (2009) Molecular phylogeny and surface morphology of marine archigregarines (Apicomplexa), *Selenidium* spp., *Filipodium phascolosomae* n. sp., and *Platyproteum* n. g. and comb. from North-Eastern Pacific peanut worms (Sipuncula). *J. Eukaryot. Microbiol.* 56, 428–439
50. Schrével, J. (1971) Observations biologiques et ultrastructurales sur les Selenidiidae et leurs conséquences sur la systématique des Grégarinomorphes. *J. Protozool.* 18, 448–470
51. Füssy, Z. *et al.* (2019) Subcellular compartments interplay for carbon and nitrogen allocation in *Chromera velia* and *Vitrella brassicaformis*. *Genome Biol. Evol.* 11, 1765–1779
52. Patten, R. (1936) Notes on a new Protozoon, *Piridium sociabile* n.gen., n.sp., from the foot of *Buccinum undatum*. *Parasitology* 28, 502–516
53. Bartošová-Sojková, P. *et al.* (2015) Epicellular apicomplexans: Parasites 'On the way in'. *PLoS Pathog.* 11, e1005080
54. Paskerová, G.G. *et al.* (2018) Fine structure and molecular phylogenetic position of two marine gregarines, *Selenidium pygospionis* sp. n. and *S. pherusae* sp. n., with notes on the phylogeny of Archigregarinida (Apicomplexa). *Protist* 169, 826–852