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► To cite this version:

Ross F Waller, Catharina Alves-De-Souza, Phillip Cleves, Jan Janouškovec, Ehsan Kayal, et al.. Comparative biology and ecology of apicomplexans and dinoflagellates: a unique meeting of minds and biology. Trends in Parasitology, 2022, 38 (12), pp.1012-1019. 10.1016/j.pt.2022.09.010 . hal-03862729

HAL Id: hal-03862729

<https://hal.science/hal-03862729v1>

Submitted on 2 Dec 2022

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1 **Comparative Biology and Ecology of Apicomplexans and Dinoflagellates: A unique meeting of**
2 **minds and biology**

3
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26

27 **Abstract**

28 The commonalities and convergences shared in apicomplexans and dinoflagellates are continuously
29 becoming more and more apparent, yet researchers across this myzozoan supergroup seldom meet
30 at scientific meetings. The Conférence Jacques Monod meeting entitled ‘From Parasites to Plankton
31 and Back: Comparative Biology and Ecology of Apicomplexans and Dinoflagellates’ sought to change
32 this. Held at the Roscoff Marine Station in France on September 5-9, 2022, researchers spanning
33 organisms, disciplines, and perspectives met to immerse themselves in the latest developments and
34 discoveries across the group. The outcome was an exciting and stimulating view of the synergies,
35 revelations and opportunities enabled by expanding one’s view and network across this vast,
36 spectacular and important biological group. In this *TrendsTalk*, the conference organizers and several
37 young researchers present a synthesis of the key outcomes of this meeting of minds and biology.

38

39 *Left column:*
40
41 [Photo "1 Waller"]
42 Ross F. Waller
43
44 [Photo "2 Alves-de-Souza"]
45 Catharina Alves-de-Souza
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47 [Photo "3 Cleves"]
48 Phillip A. Cleves
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50 [Photo "4 Janouskovec"]
51 Jan Janouškovec
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53 [Photo "5 Kayal"]
54 Ehsan Kayal
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56 [Photo "6 Krueger"]
57 Thomas Krueger
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59 [Photo "7 Szymczak"]
60 Jeremy Szymczak
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62 [Photo "8 Yamada"]
63 Norico Yamada
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65 [Photo "9 Guillou"]
66 Laure Guillou
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68 **The meeting's rationale**

69 The development of tunnel vision is a natural, almost inescapable phenomenon in most scientific
70 fields. The complexities of biological systems and the tools and theories used to investigate them
71 often lead us towards increasingly exclusive research communities, bodies of literature and suites of
72 technologies. But this comes with the danger of also constraining our thoughts, ideas, and
73 conclusions. The constant challenge of scientists is to work against such forces that can limit our
74 work, its vision and opportunities.

75 Addressing this challenge was the overarching aim of the Conférence Jacques Monod meeting 'From
76 Parasites to Plankton and Back: Comparative Biology and Ecology of Apicomplexans and
77 Dinoflagellates' held in early September at the Roscoff Marine Station on the beautiful Brittany coast
78 in France. Apicomplexans (including chromerids and colpodellids) and dinoflagellates (including
79 perkinsids and syndinians) represent two major sister lineages of unicellular eukaryotes that have
80 far-reaching impacts on both human and environmental health and function, particularly on a
81 changing planet. Collectively they form the Myzozoa whose name is derived from the common
82 apical complex structures known to be used for host cell invasion and myzocytotic feeding within
83 both lineages. However, the research communities that study these two important groups seldom
84 meet due to their general focus on either human and animal parasitic diseases or the biology and
85 ecology of aquatic systems, respectively. But as both lineages are derived from a common ancestor,
86 they maintain many shared traits. The meeting addressed six major themes to capture and explore
87 this common biology: 1) diversity, phylogeny, and biogeography, 2) life cycles and sexual
88 reproduction, 3) genome and organelle evolution, 4) cell biology and host-symbiont interactions, 5)
89 functional ecology, and 6) new model systems, tools, and databases. Under these umbrellas, a
90 remarkable spread of organisms, techniques, questions, and discoveries were presented and
91 discussed (**Figure 1**).

92

93 **Diversity is the key to understanding Myzozoa**

94 A clear theme that emerged during the meeting was how dependent our understanding of
95 myzozoan biology is on our knowledge of the diversity of organisms found in these lineages. **Figure 2**
96 represents the spectacular diversity of organisms presented as study subjects during the meeting
97 which demonstrated how much we draw on this breadth for our insights. But there are still many
98 gaps yet to fill. The keynote address by Patrick Keeling (University of British Columbia) illustrated
99 recent notable gains that have been made in our knowledge of both apicomplexans, where
100 gregarines are emerging as major components of diversity, and dinoflagellates, where new
101 heterotrophic species are also uncovering significant evolutionary trajectories. Further talks

102 illustrated how the deep-branching lineages of both groups are also expanding, with squirmids and
103 eleutherids both recently discovered as new basal groups that inform on additional diversity within
104 each major lineage. Collectively these new organisms are redefining our understanding of the
105 relationships within these groups. For example, gregarines are now recognised as multiple lineages,
106 whereas *Cryptosporidium*'s true relationship within Apicomplexa remains uncertain. Further major
107 myzozoan diversity was revealed by both Cécile Lepère (Université Clermont Auvergne) and
108 Sebastian Metz (Station Biologique de Roscoff) who showed that perkinsids, best known as parasites
109 of marine molluscs and phytoplankton, are also much more diverse than previously appreciated.
110 Evidence of perkinsids is now widely found in freshwater habitats as well as soil, which represent new
111 diverse and often habitat-specific lineages. A common theme for much of the new diversity is the lack
112 of culturability of these organisms, or even their physical observation where eDNA surveys are the only
113 evidence of their existence. This challenges our understanding of ecological roles that this myzozoan
114 diversity fulfils, and points to much work still to be done.

115

116 **Ancestral states and parallelisms**

117 From the appreciation of Myzozoan diversity, two further themes of the meeting emerged: 1) how
118 pervasive common characters are, but also 2) how parallelisms have repeatedly occurred across the
119 group. The common perception of parasitism evolving only once early in apicomplexans is
120 overturned by the discovery of the repeated emergence of parasitism in Apicomplexa presented by
121 both Patrick Keeling and Jan Janouškovec (University of Southampton). Furthermore, Sonja
122 Rueckert's (Edinburgh Napier University) address explored if some gregarines might actually be
123 mutualists providing positive benefits to their hosts rather than negative. Of course, parasitism is
124 also found throughout perkinsids and dinoflagellates. Laure Guillou (Station Biologique de Roscoff)
125 illustrated how the dinoflagellate parasite *Amoebophrya* displays superb adaptations for parasitism
126 where it invades its host, initially establishes a parasitophorous vacuole, and then remodels the
127 host's nucleus where it ultimately resides, feeds and replicates. This dinoflagellate even selectively
128 sustains the energy producing capacity of its photosynthetic host to achieve greater parasite
129 replication. The sophistication of this parasite-host interaction, and its parallels to the better studied
130 apicomplexans, reveal how dispersed such complex traits are across the group. Indeed, versatility of
131 trophic modes was a central theme of myzozoan biology and evolution explored at the meeting,
132 with multiple shifts between phototrophy, heterotrophy and parasitism found. Victoria Jacko-
133 Reynolds (University of British Columbia) showed examples of photoparasitic dinoflagellates of the
134 genus *Blastodinium* in the throes of conversion from autotrophy to parasitism, showing that these
135 shifts are contemporary and ongoing.

136 A common element of myzozoan cells that might explain these core themes of their biology is the
137 ancestral apical complex structure linked to both feeding and invasion. Dominique Soldati-Favre
138 (University of Geneva) and Markus Meissner (Ludwig Maximilians Universität) both presented
139 superb studies of the assembly, structure, and function of the *Toxoplasma* conoid and apical
140 complex using the molecular and cell biology tools that only such a well-developed model organism
141 can allow. Maryse Lebrun (Université de Montpellier) further revealed the molecular machinery for
142 rhoptry apical secretion during *Toxoplasma* invasion. Notably, her group discovered elements of this
143 machinery through its conservation with ciliates, hinting that these processes are ancient rather
144 than new. Moreover, Jeremy Szymczak (Sorbonne Université) tantalized us with images of similar
145 apical complex structures in the parasitic dinoflagellate *Amoebophyra*, and such structures have
146 been widely observed in all myzozoan groups including both parasites, predatory heterotrophs and
147 even autotrophs. Collectively these studies reveal the deep ancestry of these common cellular
148 machineries for interactions with other cells and organisms and that serve multiple different
149 lifestyles. In turn, the theme of mixotrophy, cells that are both photosynthetic and heterotrophic,
150 was discussed as greatly understudied in Myzozoa but is likely central to both the ecological
151 functions of this group and its propensity to oscillate between different trophic modes.

152 Symbiosis is another topic where parallelism was a clear theme. Fabrice Not (Station Biologique de
153 Roscoff) illustrated how the perception of Symbiodiniaceae being the primary dinoflagellate
154 symbiotic group is misleading, with lineages found across dinoflagellate diversity forming
155 partnerships with a wide variety of other organisms. Both he and Senjie Lin (University of
156 Connecticut) touched on some of the cellular and genomic adaptations seen upon entering into such
157 relationships, but both showed that this is an underexplored area where much further work is
158 needed. Myzozoan organisms as the hosts of endosymbiotic partners is another major theme of
159 diversity and parallelism in this group. The plastid in both photosynthetic and non-photosynthetic
160 myzozoans has been a topic of strong interest for several decades, but still new discoveries and
161 revisions are being made. Elisabeth Hehenberger (Czech Academy of Sciences) showed that parallel
162 loss of plastid function is ever more apparent than was realized when wider surveys of taxa are
163 made. Even parallel loss of the organelle genome or the organelle itself, both considered exceedingly
164 rare events, are now evident. Miroslav Obornik (University of South Bohemia) illustrated how we still
165 cannot even be sure of a simple ancestry of the myzozoan plastid(s). His group's work argues for
166 lateral gain of a chlorophyll *c*-containing plastid from eustigmatophytes, and possible subsequent
167 early parallel plastid replacement in dinoflagellates, as still credible possibilities. From ancient to
168 new, Noriko Yamada (University of Konstanz) demonstrated how much we can learn from recent
169 cases of plastid uptake in dinoflagellates. She has developed multiple cell models bearing nascent

170 diatom endosymbionts offering new insights into the patterns and processes of these developing
171 relationships. Similar to plastids, mitochondrial evolution in Myzozoa also follows these patterns of
172 parallelism. Varsha Mathur (University of Oxford) exploited single-cell transcriptomics of
173 unculturable gregarines to illuminate patterns of parallel functional loss in mitochondria, notably of
174 complex III and IV of the electron transport chain. Moreover, mitochondrial parallel adaptations also
175 span the group with independent fragmentation and relocation of *cox1* seemingly having occurred in
176 some gregarines (Varsha Mathur) as well as the dinoflagellate *Amoebophrya* (Ehsan Kayal, Station
177 Biologique de Roscoff).

178 In this backdrop of parallelism, resolving the state of ancestral features can be challenging. Gliding
179 motility is closely associated with parasitism in Apicomplexa, and Isabelle Tardieux (Université
180 Grenoble Alpes) dazzled us with her biophysical studies of force delivery mechanisms driving the
181 well-studied gliding patterns of *Toxoplasma*. However, some of the champions of gliding speed are
182 found in the gregarines, and genomic analysis of *Podospira* by Isabelle Florent (Muséum National
183 d'Histoire Naturelle) showed that the identifiable molecular signatures of gliding are relatively
184 limited when considered more broadly. The fascinating but open questions of when and how gliding
185 developed in Myzozoa is thus a challenge to investigate by genomics alone. Complex cell cycles are
186 another trait that reaches across all groups. Differentiated sexual stages are often key to
187 transmission and persistence, and Oliver Bilker (Umeå University) showed his use of genetic screens
188 in *Plasmodium* to identify a wide range of fertility-related genes. While sex in the nearest
189 photosynthetic relatives, *Chromera* and *Vitrella*, is less well understood, the generation of motile
190 zoospores was shown by Jitka Richtová (Czech Academy of Sciences) to be equally carefully
191 controlled and likely responsive to both metabolic and environmental signals. Jeremy Szymczak also
192 demonstrated that transmissive stages of parasitic dinoflagellates can employ distinct differentiated
193 spore forms, although the significance of these is also yet to be elucidated. Similarly, Rosa Figueroa
194 (Instituto Español de Oceanografía) summarized the lifecycle complexities of bloom-forming
195 dinoflagellates in general, and how much is still to be learned of the strategies and control of the
196 different sexual and lifecycle stages in this group. Finally, Shauna Murray (University of Technology
197 Sydney) discussed secondary metabolite production in dinoflagellates and how both gene expansion
198 and lateral gene transfer contribute to the wide range of toxins that many produce, often with major
199 impacts on food chains and ecosystems. The complex evolution of these traits, however, remains
200 difficult to unpick, and the secondary metabolism in apicomplexans is substantially unexplored,
201 further confounding comparisons or the derivation of common principles.

202

203 **Tools and technologies and the path forward**

204 A final core theme of the meeting was how new tools and technologies are driving the opportunities
205 for discovery and understanding in Myzozoa. Of course, not all organism systems are equal, and the
206 disparity was stark between those that can be cultured and genetically manipulated, versus those
207 that must be field-isolated for samples or are even only detectable as meta-genomic traces from the
208 environmental. Dominique Soldati-Favre championed the role of observation in scientific discovery,
209 and her group's use of Ultrastructure Expansion Microscopy (U-ExM) demonstrated how new
210 resolution should be achievable across the field where cells can be collected. Markus Meissner's
211 engineered filamentous actin-detecting chromobodies have also unveiled a new era for
212 understanding actin dynamics and function, and testing for conservation of these processes should
213 also now be available in all genetically transformable groups. A noteworthy breakthrough in model
214 organism development has been that for *Cryptosporidium* led by Boris Striepen's group (University
215 of Pennsylvania). Through this they provide a revised understanding of this important parasite's
216 lifecycle including sexual commitment, and knowledge of new cell compartments driving host-
217 interactions, all of which can now be interrogated through reverse genetics.

218 Sequencing technologies remain at the heart of much of myzozoan research, particularly where cells
219 cannot be cultured. Single-cell genomics and transcriptomics have enabled remarkably penetrating
220 insights, in some cases where only a few tens of cells have ever been seen and collected (e.g., the
221 eleutherids presented by Elisabeth Hehenberger). Single-cell RNA SEQ of cell populations is also
222 giving stunningly resolved detail of the transcriptional programs of lifecycles and differentiated
223 states, and these were shown in several presentations. A common challenge, however, is the 'dark
224 genetic matter', the unique genes and proteins either within myzozoan groups as a whole, or in
225 individual lineages. Isabelle Florent lamented this challenge in interpreting gregarine genomes, and
226 Lucie Bittner (Muséum National d'Histoire Naturelle) and others are tackling it with sequence
227 similarity networks (SSN), structure similarity networks (e.g., via AlphaFold), gene correlation with
228 ecosystems and biogeography, and machine learning to shed light on the 'dark proteome'. A
229 different strategy to illuminate the function of new, derived, and unstudied proteins is the 'LOPIT'
230 method of spatial proteomics employed by Ross Waller's group (University of Cambridge). This
231 method is only limited by the culturability of an organism and provides genome-level resolution of
232 the subcellular distribution of a cell's proteins, and enables comparative cell biology across Myzozoa
233 and beyond. Forward genetic screens to identify the molecules of function are also starting to be
234 applied more widely in Myzozoa. While the use of targeted mutations in *Toxoplasma* and
235 *Plasmodium* allowed screening for proteins involved in actin networks and sex functions by Markus
236 Meissner and Oliver Billker, respectively, Ugo Cenci (University of Lille) demonstrated that lack of
237 experimental genetics is not a barrier to forward genetics. Using UV-based mutation and genome

238 sequencing in *Chromera* he is identifying the genes for starch synthesis in this otherwise genetically
239 intractable system. The wide potential of 'omics' data, and increasingly its correlation with
240 'metadata', was reinforced by David Roos's (University of Pennsylvania) eloquent description of the
241 origins and current state of the VEuPathDB.org databases and tools. The challenge for Myzozoa,
242 however, is to span this entire group with integrated tools, and the importance of this was
243 recognised by all.

244 In a changing planet where myzozoan ecosystems are literally as vast as the oceans, computational
245 tools are also essential and being applied to understanding and predicting organism dynamics and
246 responses. Catharina Alves-de-Souza (University of North Carolina Wilmington) showed us how she
247 is tackling the question of how two parasites with very different parasitic strategies (*Amoebophrya*
248 and *Parvilucifera*) are able to coexist while exploiting overlapping hosts. Drawing on experimental data,
249 she showed how population modelling is required to identify the complex roles of both biotic and
250 abiotic factors that shape the dynamics of these systems. Cécile Jauzein (IFREMER) further explored
251 how host programmed cell death and generation of allelopathic compounds might be further
252 incorporated into these models. Both presentations stress the importance of assessing host-parasite
253 dynamics in plankton assemblages from a community point of view instead of relying on the pairwise
254 comparison based on networking analyses of metabarcoding data. Even Garvang (University of Oslo)
255 similarly built epidemiological models to predict the best experimental strategies to study the impacts
256 of parasitic dinoflagellates on copepods. In doing so, he reminded us that copepods are the most
257 abundant arthropods on the planet and enormously important for ocean food webs. Finally, Raffaele
258 Siano (IFREMER) stunned the audience by describing how he has developed methods to revive
259 dinoflagellate cysts from sediments over 150 years old. His group pursue paleoecology studies that
260 integrate revived dinoflagellates and their physiology examination, with sediment DNA sequencing and
261 metabolomics. Using these tools, they have been able to determine the impacts on coastal protist
262 communities by major historical environmental disturbances such as World War II and changing
263 agricultural practices affecting the Brittany coast.

264

265 **Perspectives and outstanding challenges**

266 While this report cannot comprehensively cover all the wonderful biology and science that was
267 presented at this meeting, nor fully convey the excitement of many for this convergence of systems
268 and minds, it seeks to illustrate the success of bringing diverse researchers working across myzozoan
269 biology together. The wealth of shared biology was obvious when viewed en masse. But it was also
270 clear that the interpretations that we make in individual groups are rarely complete without
271 recognition of equivalent or differing states amongst the relatives. It was powerful to see how

272 different tools have been developed, adapted, and exploited across different systems, and there is
273 clear potential for the wider application of many of these tools and techniques across this group.
274 New partnerships were formed, and it was pleasing to observe one *Plasmodium* researcher slipping
275 a dinoflagellate culture in their luggage before departure. But the challenges were also brought into
276 focus. There is vast diversity still to be discovered and/or identified at an organism level, and gaps in
277 our interpretation of this important group will remain while this is the case. For example, much of
278 the Marine Alveolate (MALV) groups remain completely uncharacterized, and predatory
279 heterotrophs are also shown to be under-sampled and under-studied in general. The limited
280 culturability of many taxa is a huge challenge, as is the lack of widely available experimental genetic
281 tools, and these are challenges that we must continue to tackle. While much biology is shared, the
282 lineage-specific differences must also be accounted for and understood, with challenges of
283 interpreting the aberrant molecular genetics of dinoflagellates and perkinsids one example and
284 theme of several presentations. This field is exciting and spectacular and there is still so much work
285 to be done. And it is with great excitement that we announce that organizers of Conférence Jacques
286 Monod have now offered to host this meeting on an ongoing three-year cycle. If you missed out this
287 time, be sure not to for the next one in 2025.

288

289 **Acknowledgements**

290 We thank the Gordon and Betty Moore Foundation for sponsoring this meeting.

291

292 **Figure 1. Word cloud of key terms listed in titles and abstracts from across the meeting.** Created
293 with wordclouds.com.

294

295 **Figure 2. The diversity of a meeting.** Phylogeny of major clades of Myzozoa: dinoflagellates (green),
296 perkinsids (red) and apicomplexans (orange), showing in enlarged bold font all the organisms that
297 were subjects of presentations during the course of the meeting. Even further diversity was
298 presented in the form of undescribed but major myzozoan clades currently known only from meta-
299 genomic sequence data.

300