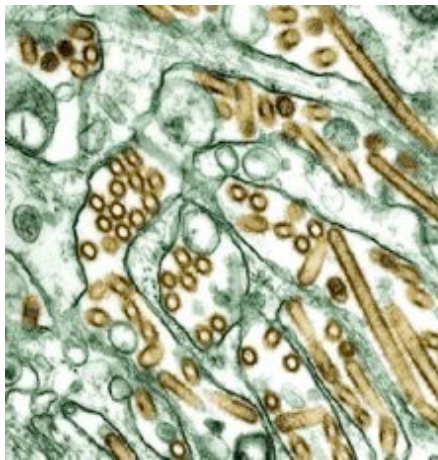


## 11. Coevolution

In January 2006, the news where full of bad news about the spread of avian influenza ('bird flu'). The WHO released details of a new mutation found in the H5N1 viruses (Figure 11.1) from Turkish birds. This genetic change results in a substitution in a virus protein that helps the flu virus to bind to receptors on host cells. It is known to increase the affinity of the virus for human receptors over poultry ones, and is also known to increase the affinity for receptors in the nose and throat rather than the lower respiratory tract. This increases the risk of human-to-human transmission. Importantly, avian influenza is at this time still a bird disease. However, what we seem to observe here is the beginning of adaptation to a new host species, humans. As yet, any evolutionary counter-adaptations on the side of this new host are unlikely, since there is no common evolutionary history of this virus with humans. By contrast, there might be evolutionary adaptations of birds to the virus. Only if there are adaptations on both sides, the pathogen and the host, we can speak of coevolution.



**Figure 11.1** An electron micrograph of H5N1 viruses 'bird flu' viruses.

### *Definitions of coevolution*

Coevolution can be defined as follows:

“Coevolution happens when two (or more) species influence each other’s evolution.”

or: “Coevolution is a process of *reciprocal evolutionary change* in interacting species.”

We will see later that also broader definitions are used, including coevolution below the level of species. The theory of coevolution is a fascinating and powerful field of evolutionary biology. Studying host-parasite coevolution may e.g. supply us with relevant tools to predict the spread and the virulence of diseases. However, at the same time, our understanding of coevolution is often still in a very initial phase. Hard evidence for coevolution is difficult to get, and we will see that there are only very few good examples that really demonstrate reciprocal evolutionary change.

### 11.1. Types of coevolutionary interactions

Coevolution implies that two species interact. Based on the benefits and costs of such interactions, they can be classified as shown in Table 11.1. Species interactions can also be classified on a scale from ‘tight’ to ‘diffuse’, based on the frequency of the interaction and the impact of the interaction on reproductive success. The more frequent, and the stronger the

fitness effects, the ‘tighter’ is an interaction. For instance, host-parasite interactions are often tight, predator-prey interactions can be rather diffuse.

**Table 11.1** Types of coevolutionary species interactions

	+	0	-
+	<p><b>Mutualism</b> Müllerian mimicry Plant-pollinator</p>		
0	<p><b>Commensalism</b> Batesian mimicry</p>	×	
-	<p><b>Antagonism</b> Aggressive mimicry Parasitism Predation Herbivory</p>		<p><b>Competition</b></p>

### **Examples of coevolution: mimicry**

The classical examples of mimicry illustrate nicely different types of co-evolutionary interactions. *Müllerian mimicry*<sup>17</sup> describes the convergence of unpalatable models to a similar phenotype, i.e. reciprocal evolution between species all of which are distasteful. It is thus characterised as a +/+ mutualistic interaction, i.e. all involved species benefit (Figure 11.2).

*Batesian mimicry*<sup>18</sup> describes the convergence of a palatable species to unpalatable models. A non-toxic, edible species mimics the warning colour of a toxic, noxious model. This is a 0/+ interaction, because only one species benefits (Figure 11.3). The system works well as long as the mimic does not become too frequent. Otherwise, the noxious model may have a disadvantage (i.e. the interaction may turn into antagonism, -/+), because predators do not avoid the warning colour any more. We will see that such *frequency dependence* is often an important element of coevolutionary interactions.

There is another form of mimicry, called *aggressive mimicry*, which describes an antagonistic -/+ interaction. Figure 11.4 shows an example, where a mutualistic cleaning symbiosis is exploited by an aggressive mimic.

<sup>17</sup> Müller, F. (1879) *Ituna* and *Thyridis*: a remarkable case of mimicry in butterflies. Proceedings of the Entomological Society of London 1879: 20-9.

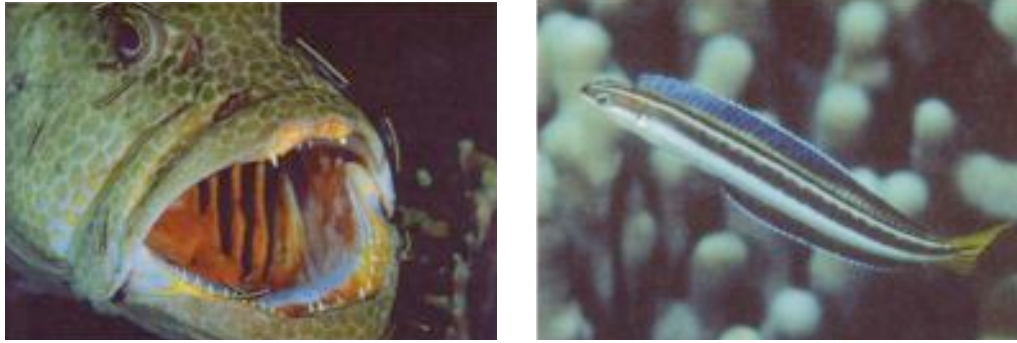
<sup>18</sup> Bates, H.W. (1862) XXXII. Contributions to the insect fauna of the Amazon valley. Lepidoptera:Heliconidae. *Transactions of the Linnean Society of London* 23: 495-566.



**Figure 11.2** Müllerian mimicry. Geographical races of *Heliconius* species, and some other Nymphalidae, all of which are distasteful, form parallel sets of Müllerian mimics.



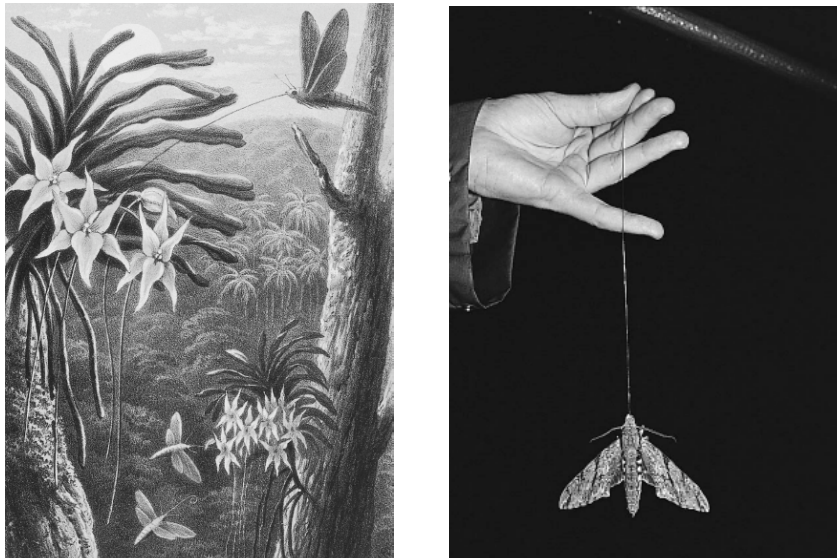
**Figure 11.3** Batesian mimicry. The mocker swallowtails of Africa (*Papilio dardanus*) are one of the most remarkable cases of Batesian mimicry known. The females mimics different toxic models in different geographical regions, with the result that they look very different both from the males of their own species and from the females of their species in other geographical regions. The males are not mimics, and on Madagascar, where no toxic models are available, the females are not mimics and resemble the males. Top row: Left, male; right, female from Madagascar. In the remaining rows the mimicking female is on the left and the toxic model is on the right of each pair.



**Figure 11.4** Left: Tiger grouper being cleaned by several cleaner wrasses (Photo D. Matthews). Right: Saber-toothed blenny, an aggressive mimic that closely resembles cleaner wrasses but, instead of removing parasites, bites a chunk out of the grouper and flees (Photo R. Fenner).

## 11.2. Evidence of coevolution

Description of coevolution has a long history. Charles Darwin already described *plant-pollinator coevolution*. He emphasized the importance of “mutual interactions of organisms” and described how coevolution may take place between bees and clover<sup>19</sup>. Darwin also wrote a book on pollination biology of orchids, where he described many specialized interactions between orchids and insects<sup>20</sup>. He depicted the Star orchid (*Angraecum sesquipedale*) from Madagascar, which has 25 cm long flower spur. He thus predicted that an insect with a matching long tongue should exist (Figure 11.5). In 1903, the Hawk moth *Xanthopan morgani praedicta* was described, but it was not before 1997 that L.T. Wasserthal could observe the predicted pollination mechanism. However, he suggested an alternative hypothesis for the coevolutionary process!<sup>21</sup>



**Figure 11.5** Left: Darwin’s predicted pollination of the star orchid of Madagascar as illustrated in an article by Wallace. Right: *Xanthopan morgani praedicta*, the longest-tongued hawkmoth of the Old World (Photo B. Pettersson & A. Nilsson).

<sup>19</sup> Darwin, C. (1859) *On the origin of species by means of natural selection*. Murray, London.

<sup>20</sup> Darwin, C. (1862) *On the various contrivances by which British and foreign orchids are fertilised by insects, and on the good effects of intercrossing* 1-vi, 365, [361] J. Murray, London.

<sup>21</sup> Wasserthal, L.T. (1997) The pollinators of the Malagasy star orchids *Angraecum sesquipedale*, *A. sororium* and *A. compactum* and the evolution of extremely long spurs by pollinator shift. *Botanica Acta* 110, 343-359

Let us first catch on the original hypothesis of orchid-moth coevolution, as proposed by Darwin and Wallace: The basic idea is that an orchid evolves a long spur to ensure that only specialised pollinators can get access to nectar. A pollinator species evolves a long tongue, and will thus specialise on this plant. This pollinator will therefore always visit the same flower species, thus effectively pollinate it, which is beneficial for the orchid. By contrast, Wasserthal suggested a different way how the long spur and the long tongue could have evolved rather indirectly. His idea is that there is first

Predator-moth *coevolution* which is followed by plant *coadaptation*. He suggests that moths evolved long tongues to increase distance-keeping and sideways oscillation hawking while nectar feeding, as an adaptation to avoid predation by bats from the air and in particular by spiders sitting on the orchid. Plants then “follow” and evolve long spurs, thereby bringing their pollen closer to the moth. Who is right? Honestly, we don’t know yet! Still more research would be needed to clarify this issue. The example shows an important principle: *Coadaptation suggests, but is not conclusive evidence of coevolution!* Full evidence of coevolution (i.e. reciprocal change in interacting species) is hard to obtain. In the following, we will now get to know several examples that demonstrate ways to obtain (partial) evidence of coevolution.

### ***Evidence from experiments***

Figure 11.6 shows an ant (*Formica fusca*) feeding on the caterpillar of the lycaenid butterfly *Glaucopsyche lygdamus*. The ant drinks ‘honeydew’ from a special organ (Newcomer’s organ), which provides food for the ants. Why do the caterpillars feed the ants? Pierce & Mead (1981)<sup>22</sup> carried out an experiment where they excluded ants from the caterpillars. This resulted in much higher parasitisation, indicating that ants benefit from protection by the ants against parasitoids (Figure 11.6). The experiment thus demonstrates a case of mutualism between ants and caterpillars.



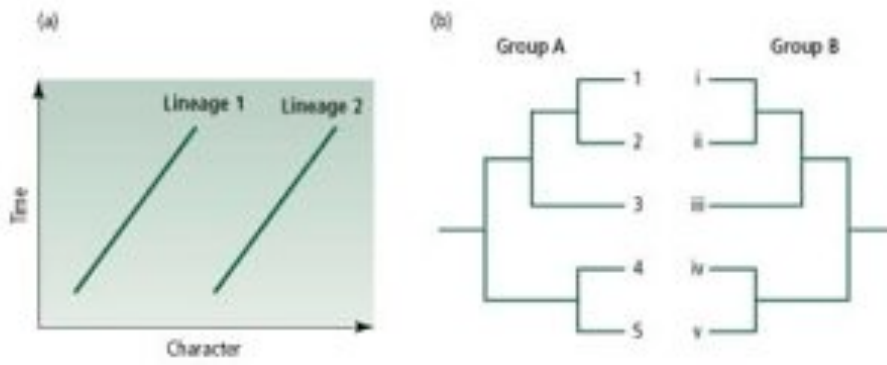
**Figure 11.6** Complimentary coadaptations in an ant and caterpillar. (a) The ant is drinking honeydew from a caterpillar of *Glaucopsyche lygdamus*. (b) The ant defends a caterpillar against a parasitic braconid wasps.

### ***Evidence from macroevolution***

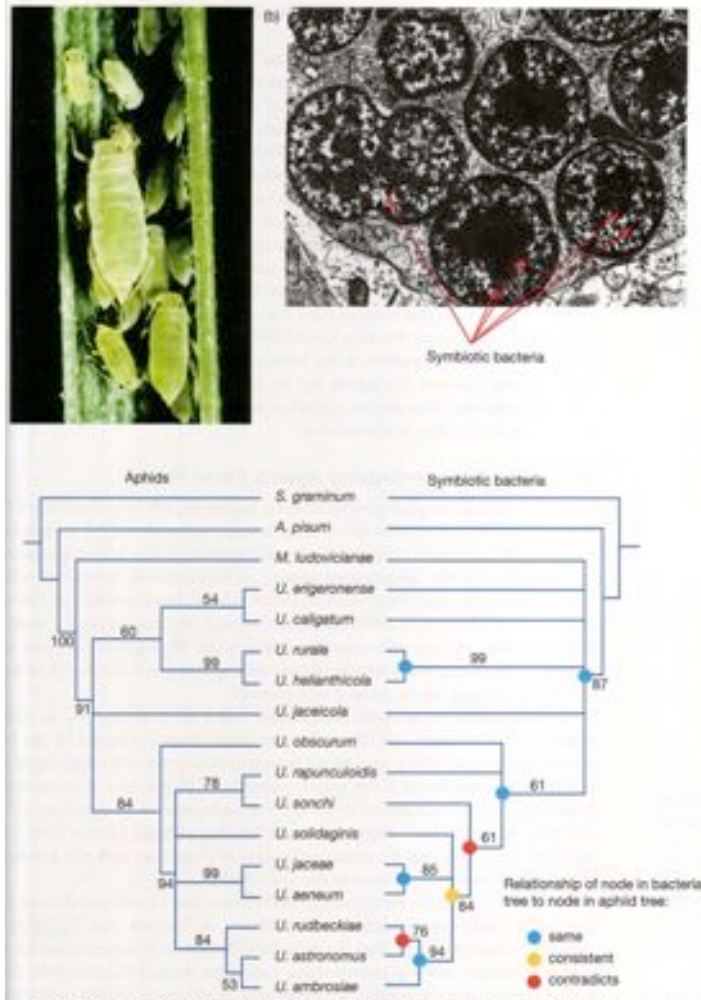
Macroevolution describes the pattern of evolution at and above the species level. Research makes use of the fossil history and of systematics. Identified taxonomic relationships can give valuable hints that coevolution might have played a role. If two lineages mutually influence each other’s evolution, they might tend to change (a) and speciate (b) together (Figure 11.7). This might result in cophylogenies. **Error! Reference source not found.** shows an example of aphids and their bacterial endosymbionts, which seem to speciate together. They show, at least partly, mirror-image phylogenies.<sup>23</sup>

<sup>22</sup> Pierce, N.E. & Mead, P.S. (1981). Parasitoids as selective agents in the symbiosis between lycaenid butterfly larvae and ants. *Science* 211: 1185-1187.

<sup>23</sup> Clark, M.A., *et al.* (2000) Cospeciation between bacterial endosymbionts (*Buchnera*) and a recent radiation of aphids (*Uroleucon*) and pitfalls of testing for phylogenetic congruence. *Evolution* 54, 517-525



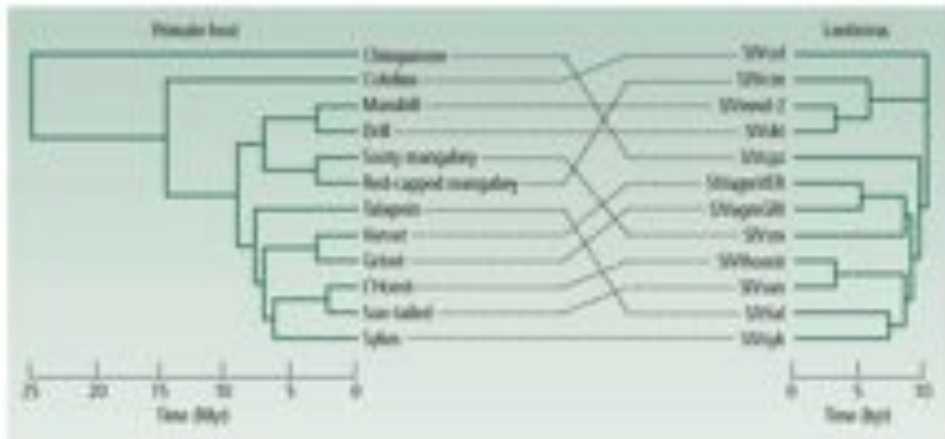
**Figure 11.7** Cophylogenies as evidence for coevolution. The two lineages tend to (a) change together, and (b) speciate together.



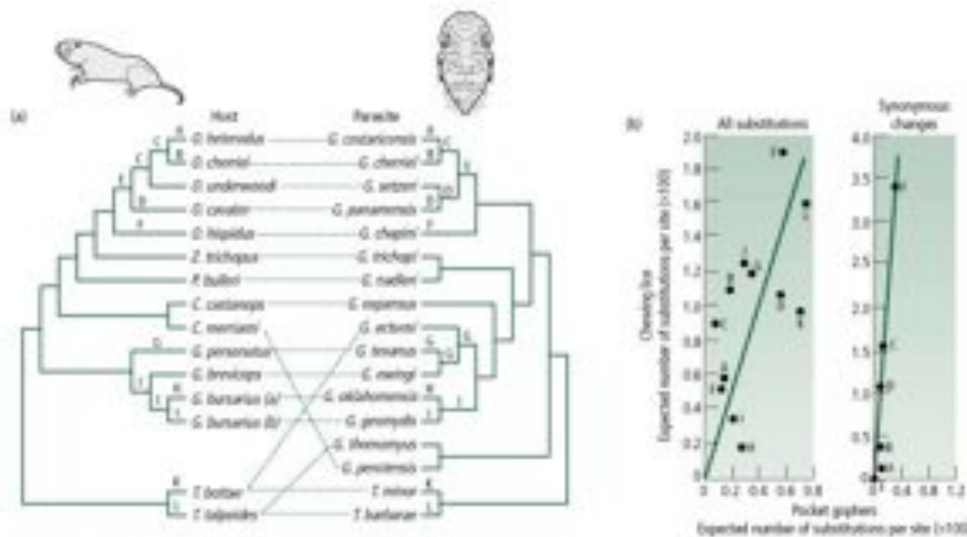
**Figure 11.8** Did aphids (left) and their bacterial endosymbionts (right) speciate together? Phylogenetic analysis shows that most nodes in the trees support cospeciation.

However, cophylogenies are not always proof of cospeciation. Figure 11.9 shows an example of primate hosts and lentivirus. Although there are cophylogenies, the time scale shows that the species did not split together. Instead, viruses may have switched preferentially between host species that are closely related, thereby creating the mirror-image phylogeny. By contrast, in pocket gophers and louse, mirror-image phylogenies coincide with simultaneous speciation, as supported by substitution rates of nucleotides (Figure 11.10).<sup>24</sup> Together, this gives good evidence of coevolution.

Cophylogenies may even affect more than two interacting taxa, as in the ancient “tripartite” coevolution of leafcutter ants, their food fungus and a pathogenic fungus. The ant, the cultivated food fungus and the parasitic fungus show partly mirror-image phylogenies (Figure 11.11). There is even a fourth party involved, which is a bacterium that produces antifungal agent.

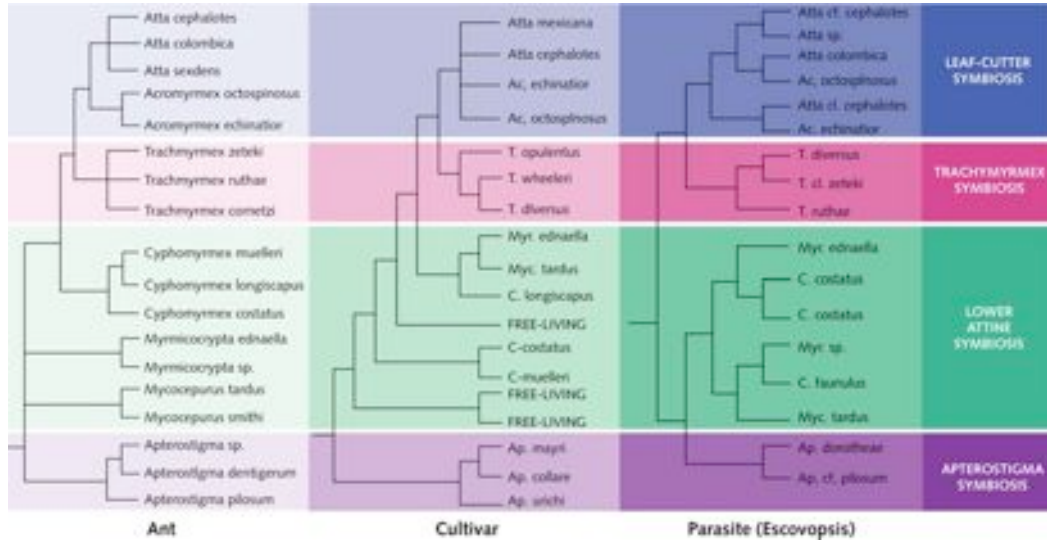


**Figure 11.9** Phylogenies of primate hosts and primate lentiviruses. The timescale of the phylogenies, based on the ‘molecular clock’, shows the different timing of the splits in the two taxa.



**Figure 11.10** (a) Mirror image phylogenies in pocket gophers (*Geomyidae*) and their mallophagan parasites. (b) Test of simultaneity of speciation from the estimated number of base substitutions. The clocks in the two taxa run at different rates because of differences in generation times. The fit is better when only synonymous changes are counted.

<sup>24</sup> Hafner, M.S., *et al.* (1994) Disparate Rates of Molecular Evolution in Cospeciating Hosts and Parasites. *Science* 265, 1087-1090



**Figure 11.11** The tripartite coevolution of leafcutter ants (left), their cultivars (middle), and the pathogen of their cultivars (right).

As an aside, we here briefly address the question: How informative are phylogenetic data? When we use phylogenies, the number of nodes (independent splits) is relevant, thus determining the sample size for the statistical analysis. A statistic based on this construction is the ‘Method of phylogenetic independent contrasts’. Figure 11.12 shows an example where the hypothesis was tested that species diversity is higher when pollination is biotic (by pollinators) rather than abiotic (e.g. by wind). Instead of simply comparing the number of species with biotic and abiotic pollination, we need to identify nodes (branching points) where two sister branches have contrasting means of pollination, and compare the species number between the two modes of pollination for each of those nodes.

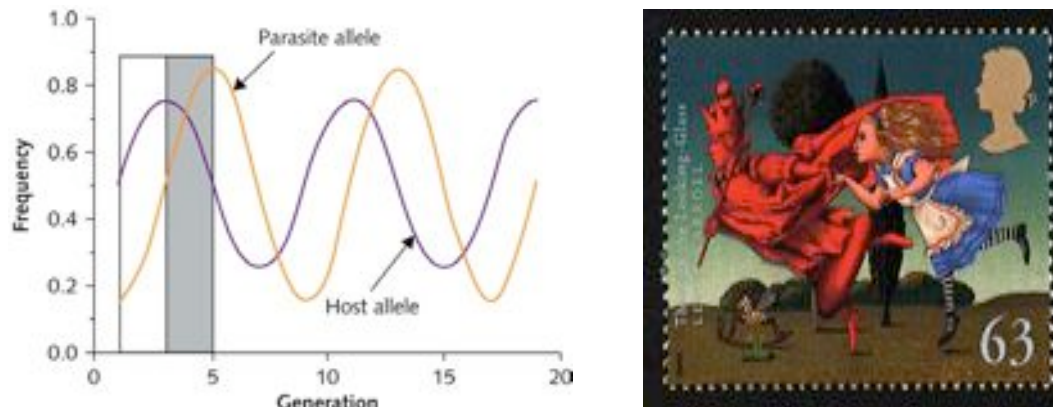


**Figure 11.12** Testing the effect of biotic as opposed to abiotic pollination on species diversity, using phylogenetically independent trials. Here, two nodes provide independent contrasts.



### *Evidence from microevolution*

Microevolution is the process of evolution within populations. Since this process is acting on a rather rapid timescale, and since we can in principle directly study genetic changes that are indicative of evolutionary change, microevolution should provide good tests of coevolution. However, in practice good microevolutionary evidence for coevolution is still largely lacking. A field that has seen particularly intense discussion in this regard is host-parasite coevolution. According to theory, we might expect coadaptational cycles of parasite and host allele frequencies that are based on *frequency-dependent selection* (Figure 11.13).



**Figure 11.13** Left: Cycling of parasite and host allele frequencies as a result of frequency-dependent selection. Right: Such coevolutionary processes have been denoted as the ‘Red Queen dynamics’.

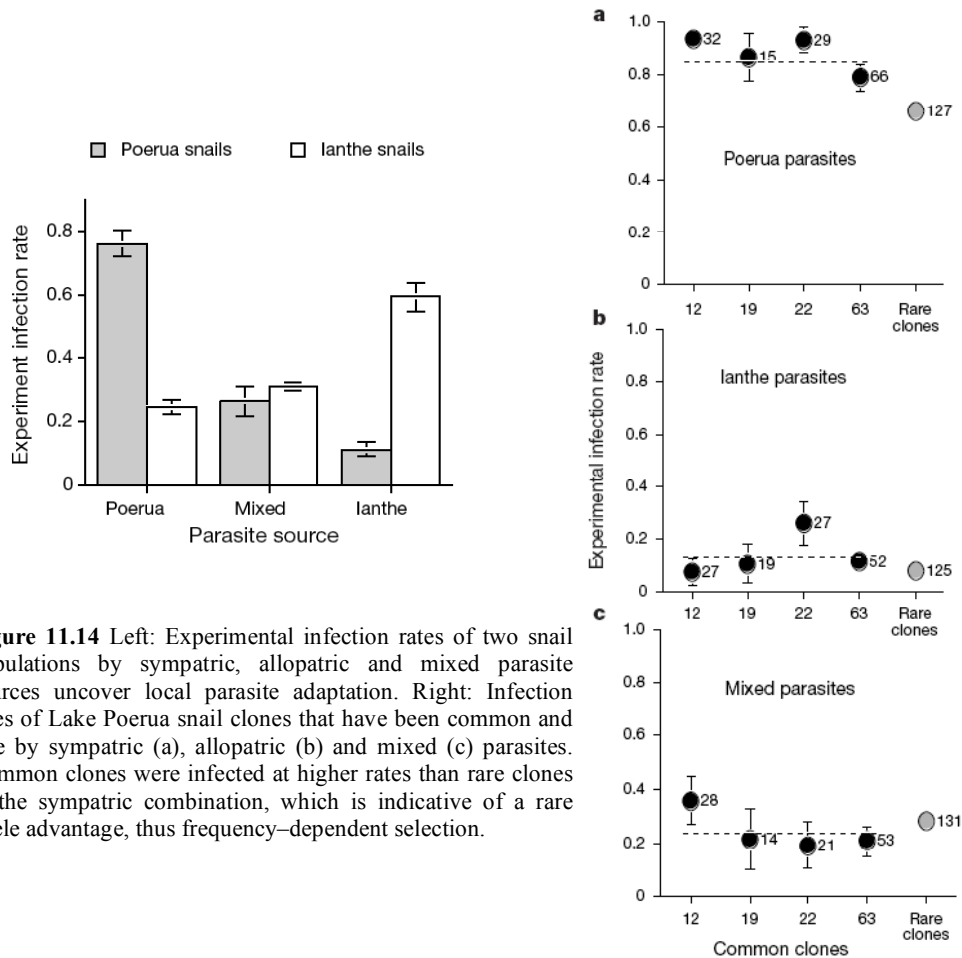
Dynamics of host-parasite coevolution have been described with the ‘Red Queen hypothesis’. The core idea is that hosts and parasites never stand still. There is constant evolutionary change, that is adaptation of one part, e.g. the parasite, will almost inevitably lead to counter-adaptation on the other side, the host, potentially resulting in a never-ending arms race. Why is this hypothesis called the Red Queen?<sup>25</sup> This is based on the observation to Alice by the Red Queen in Lewis Carroll's tale ‘Through the Looking Glass’ that “(...) in this place it takes all the running you can do, to keep in the same place.”

In the context of host-parasite coevolution, the moving environment is the evolving parasite. Parasites are expected to evolve more rapidly than their host, because they have a greater relative evolutionary potential. In principle, we can expect that, during coevolution, the interacting species with (i) the shorter generation time, (ii) more genetic variation for the interaction trait, and (iii) sexual reproduction will evolve more rapidly. Therefore, the ‘Red Queen hypothesis’ is mainly a well-received explanation for the maintenance of sexual reproduction (see chapter 12).

Despite its conspicuousness and intensive theoretical treatment, clear evidence that the Red Queen works in natural systems is still scarce. Among the best examples are studies on snails *Potamopyrgus antipodarum* and their trematode parasites *Microphallus* spec. in New Zealand (Figure 11.14).<sup>26</sup> Several expectations from the Red Queen hypothesis were supported in this system. If parasites are ahead in the arms race, then sympatric (i.e. local) parasites should be superior to allopatric ones. Such *local adaptation* of parasites was found. Moreover, under frequency-dependent selection we might expect an advantage of rare host clones, which could also be demonstrated.

<sup>25</sup> van Valen, L.E.T. (1973) A new evolutionary law. *Evolutionary Theory* 1: 1-30.

<sup>26</sup> Lively, C.M., and Dybdahl, M.F. (2000) Parasite adaptation to locally common host genotypes. *Nature* 405, 679-681



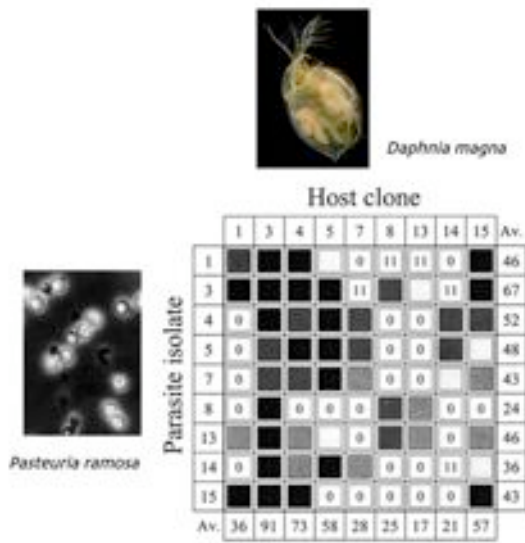
**Figure 11.14** Left: Experimental infection rates of two snail populations by sympatric, allopatric and mixed parasite sources uncover local parasite adaptation. Right: Infection rates of Lake Poerua snail clones that have been common and rare by sympatric (a), allopatric (b) and mixed (c) parasites. Common clones were infected at higher rates than rare clones in the sympatric combination, which is indicative of a rare allele advantage, thus frequency-dependent selection.

### 11.3. Dynamics of coevolution

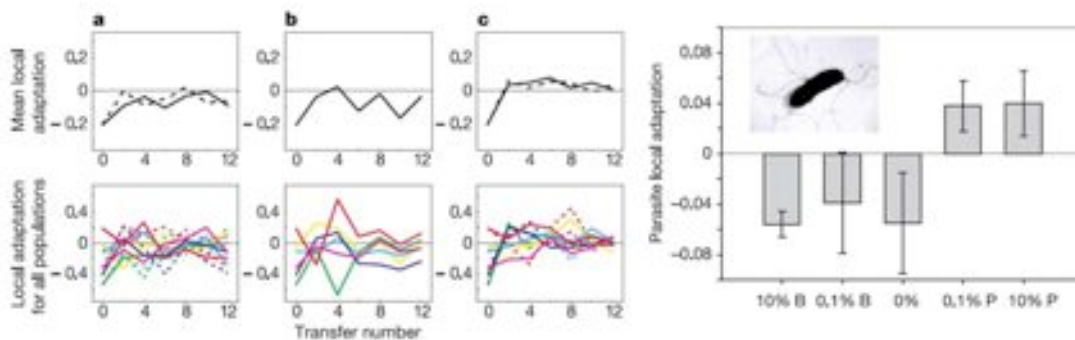
The previous example already showed that coevolutionary interactions are very dynamic in time, and that such dynamics in time may translate into spatial differences, in particular local adaptation. If we would take a snapshot in time of a coevolving host-parasite system, we expect that certain host genotypes are particularly susceptible to certain parasite genotypes and *vice versa*. Such specific host X parasite interactions have been observed (Figure 11.15).<sup>27</sup> They deliver suggestive genetic evidence for dynamic specific interactions. Theory predicts that migration (as a source of genetic variation) enhances local adaptation, as long as it does not completely homogenize populations. Experimental proof for this notion comes from bacteriophage parasites of *Pseudomonas fluorescens* (Figure 11.16).<sup>28</sup>

<sup>27</sup> Carius, H.J., *et al.* (2001) Genetic variation in a host-parasite association: Potential for coevolution and frequency-dependent selection. *Evolution* 55, 1136-1145

<sup>28</sup> Morgan, A.D., *et al.* (2005) The effect of migration on local adaptation in a coevolving host-parasite system. *Nature* 437, 253-256



**Figure 11.15** Genotype-specific host x parasite interactions Percentage infected hosts in all 81 host clone-parasite isolate combinations of 9 host clones and 9 parasite isolates. Percentage of hosts infected (usually of nine replicates) are indicated by the gray shading. For the lowest infection range (0–20%), the actual infection percentage is given to distinguish between zero and low infection rates. The bottom row and most right column (labeled Av.) of each table shows the average percentage of infected hosts.



**Figure 11.16** The effect of differential migration rates on local adaptation. Left: Parasite local adaptation is shown through time for individual populations (bottom) and for the average over the different populations (top). a, Host migration only; b, no migration; c, parasite migration only. In a and c, solid lines show 10% migration, dashed lines 0.1% migration. Right: Mean local adaptation of parasites. Data are averaged over six populations and six time points (T2, T4, T6, T8, T10 and T12) for different migration treatments. Results are means and s.e.m. across populations. P, phage migration; B, bacterial migration. These results show that, in the absence of migration, parasites tend to be locally maladapted. However, parasite migration results in parasite local adaptation, but host migration alone has no significant effect.

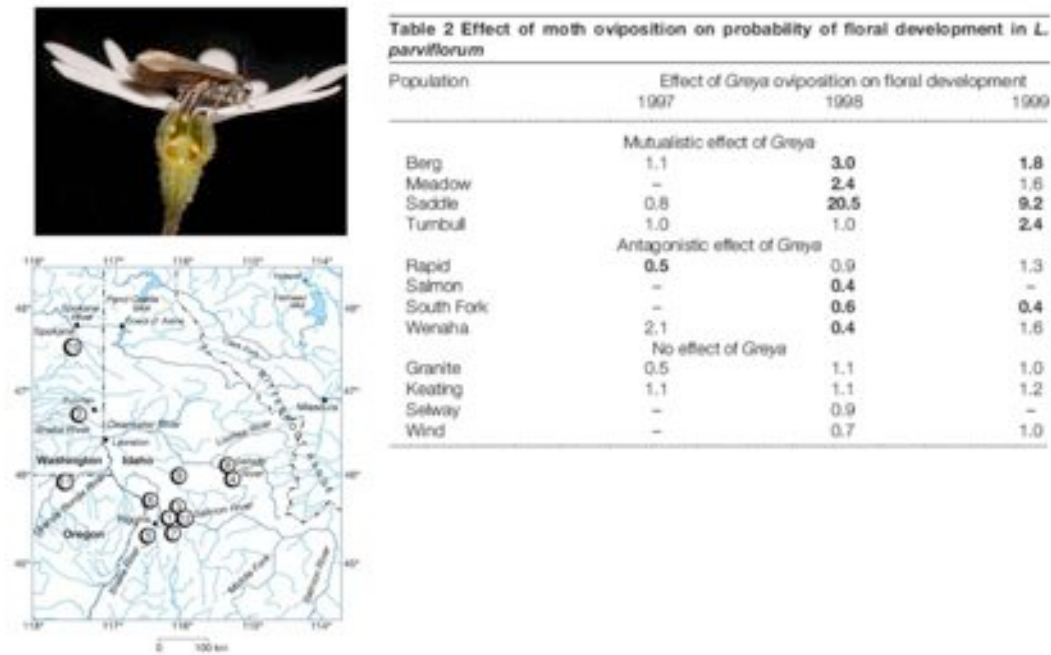
### *A geographic mosaic of adaptation*

These observations can be incorporated into a more general theory, the so-called ‘Geographic mosaic theory of coevolution’. This is based on geographic differences in species interactions due to:

- variation between habitats in natural selection
- a constantly changing genetic landscape shaped by gene flow and other forces
- reciprocal selection in only some communities (coevolutionary hotspots)

This heterogeneity can lead to the extreme case that species interactions can be mutualistic in some habitats, but commensal or even antagonistic in others (Figure 11.17).<sup>29</sup>

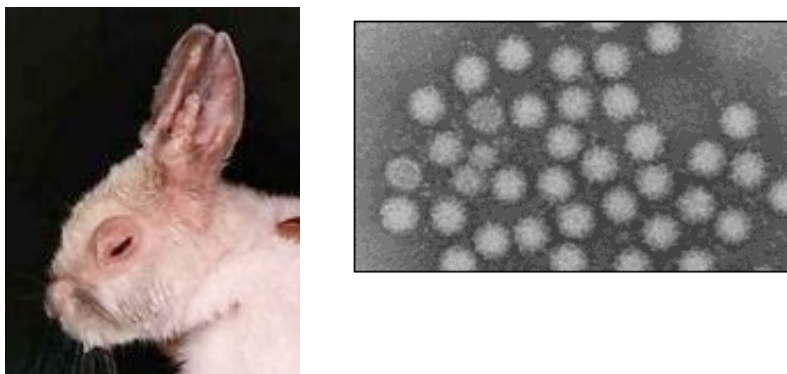
<sup>29</sup> Thompson, J.N., and Cunningham, B.M. (2002) Geographic structure and dynamics of coevolutionary selection. *Nature* 417, 735-738



**Figure 11.17** Top left: The moth *Greya politella* oviposits into the flowers of the plant *Lithophragma parviflorum*. The flower is thereby pollinated, but moth offspring feed on the plant. Whether or not this interaction is beneficial to the plant depends on the availability of alternative pollinators. Bottom left: Distribution of study sites for analysis of coevolutionary hotspots in the interaction between the plant *Lithophragma parviflorum* and the moth *Greya politella*. Right: Results are shown as the ratio of the percentage of developed capsules containing eggs to the percentage of aborted capsules containing eggs. Significant effects are shown in bold. Values significantly >1 indicate selective development of capsules containing eggs. Values significantly <1 indicate selective abortion of capsules containing eggs. These results show that the interaction can be highly divergent across both narrow and broad geographic scales, thereby fuelling continuing coevolution of taxa.

### *Evolution of virulence*

As an aside, we want to address briefly one important aspect of the dynamics of coevolution: the evolution of virulence. A famous example is the *Myxoma* virus that was introduced to Australia to reduce the rabbit, which had reached extremely high densities and which was regarded as a pest species (Figure 11.18). It was found that within a few years, the virus reduced its virulence to an intermediate value. Also, the rabbits evolved partial resistance (Table 11.2).



**Figure 11.18** Rabbit (left) infected with the *Myxoma* virus (right).

**Table 11.2** Top: The myxoma virus has evolved towards lower, intermediate virulence after its introduction to Australia. Bottom: Rabbits have evolved resistance after the introduction of the myxoma virus.

Country	Virulence grade					
	I	II	III A	III B	IV	V
<b>Australia</b>						
1950-51	100	0	0	0	0	0
1958-59	0	25	29	27	14	5
1963-64	0	6.3	26	34	31.3	8.3
<b>France</b>						
1953	100	0	0	0	0	0
1962	11	19.3	34.6	20.8	13.5	0.8
1968	2	4.1	14.4	20.7	58.8	4.3
<b>Britain</b>						
1953	100	0	0	0	0	0
1962-67	3	15.1	48.4	21.7	10.3	0.7
1968-70	0	0	78	22	0	0
1971-73	0	3.3	36.7	56.7	3.3	0
1974-76	1.3	23.3	55	11.8	8.6	0
1977-80	0	30.4	56.5	8.7	4.3	0

	Melive		Gippsland	
	Number tested	Mortality (%)	Number tested	Mortality (%)
Unselected rabbits		100		100
<b>Selected rabbits</b>				
1961-66	241	68	169	94
1967-71	119	66	55	90
1972-75	72	67	482	85

Does this example show that parasites always become benign to their hosts on the long term? For a long time, people thought so, however, this view is not correct. Although virulence must be seen as a trait that is shaped by host and parasite, the main clue to understanding virulence evolution is the fitness of the parasite, with the basic reproductive rate  $R_0$  as an important magnitude:

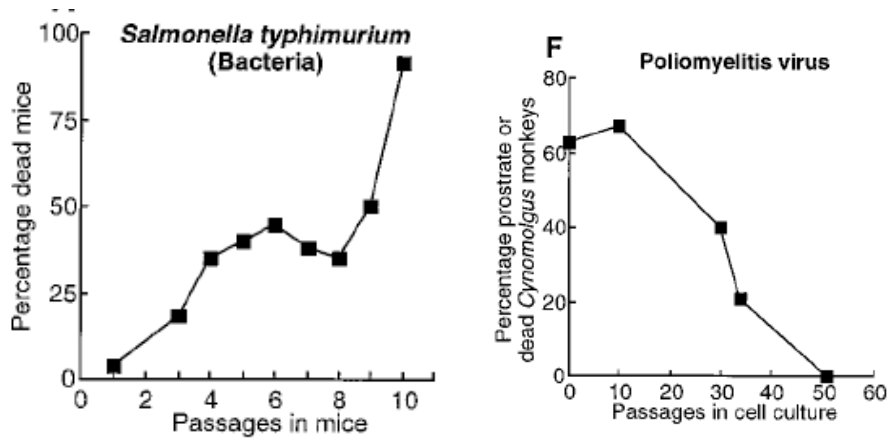
$$R_0 = \frac{\beta(\alpha) \times N}{\mu + \alpha + \nu}$$

with:

- $R_0$  basic reproductive rate of parasite
- $\beta$  transmission
- $N$  host population size
- $\mu$  background mortality
- $\alpha$  parasite-induced mortality
- $\nu$  host recovery rate

Note that transmission  $\beta$  is a function of parasite-induced host mortality  $\alpha$ . This will often mean that parasites face a trade-off between within-host and between-host components of fitness, i.e. more growth or replication within a host is often associated with higher host mortality and thus reduced transmission to the next host. Reduced transmission may result from host mortality or morbidity. Parasites that are *vertically transmitted* (from mothers to offspring) harm themselves when they strongly reduce the fitness (i.e. offspring production) of their host. They therefore have generally lower virulence than parasites that are transmitted *horizontally* in a population. Another important aspect is *within-host competition*, which might lead to higher virulence especially when the competitors are unrelated.

Experimental evolution of virulence in *serial passage experiments* (SPEs) is an interesting tool to study virulence.<sup>30</sup> Parasites are used to experimentally infect a host, extracted from the host, and then used to infect the next host, etc. This means that the parasites can adapt to their host, while the hosts cannot. Serial passage in a new host strain often increases virulence there, but decreases virulence in the former host (Figure 11.19). Such attenuation, e.g. in cell cultures, is also used for vaccine development.



**Figure 11.19** Examples of the change in virulence (left) and attenuation (right) during SPEs.

Why does virulence often increase in SPEs? The following reasons have been hypothesized, all of which could be true in one or the other system.

- *Parasite competition*  
 Passed parasites pay no costs for killing the host because transmission relies on the experimenter. Thus, within-host competition selects for virulent parasite variants irrespective of their effect on host survival.
- *Parasite life-history trade-off*  
 Increased investment to within-host growth rates, because between-host transmission stages are not needed during SPEs.
- *Host diversity*  
 Hosts in SPEs are usually of low genetic diversity or even clonal, parasites may achieve high virulence because they adapt to specific host genotypes (cf. Red Queen).

<sup>30</sup> Ebert, D. (1998) Evolution - Experimental evolution of parasites. *Science* 282, 1432-1435

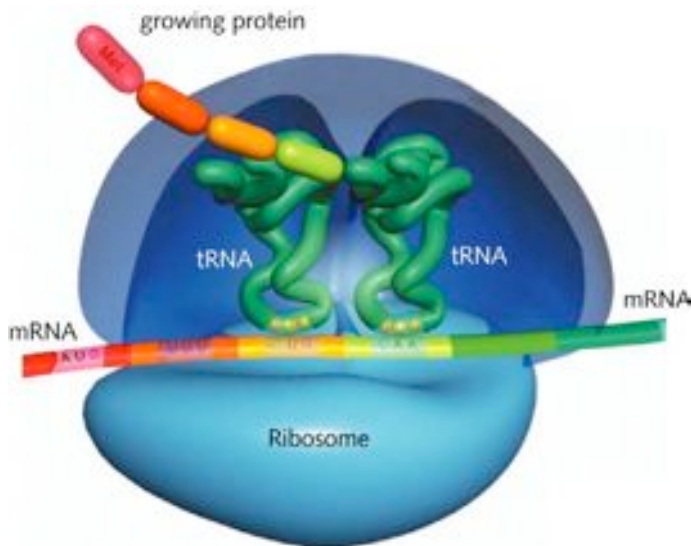
### 11.4. Levels of coevolution

We will now broaden our original definitions of coevolution as follows:

“Coevolution is a process of reciprocal evolutionary change in interacting *entities*.”

Here, entities could be species, but also other levels, such as nucleotides, amino acids, proteins, genomes, proteomes, organisms and perhaps even ecosystems (although the latter is controversial).

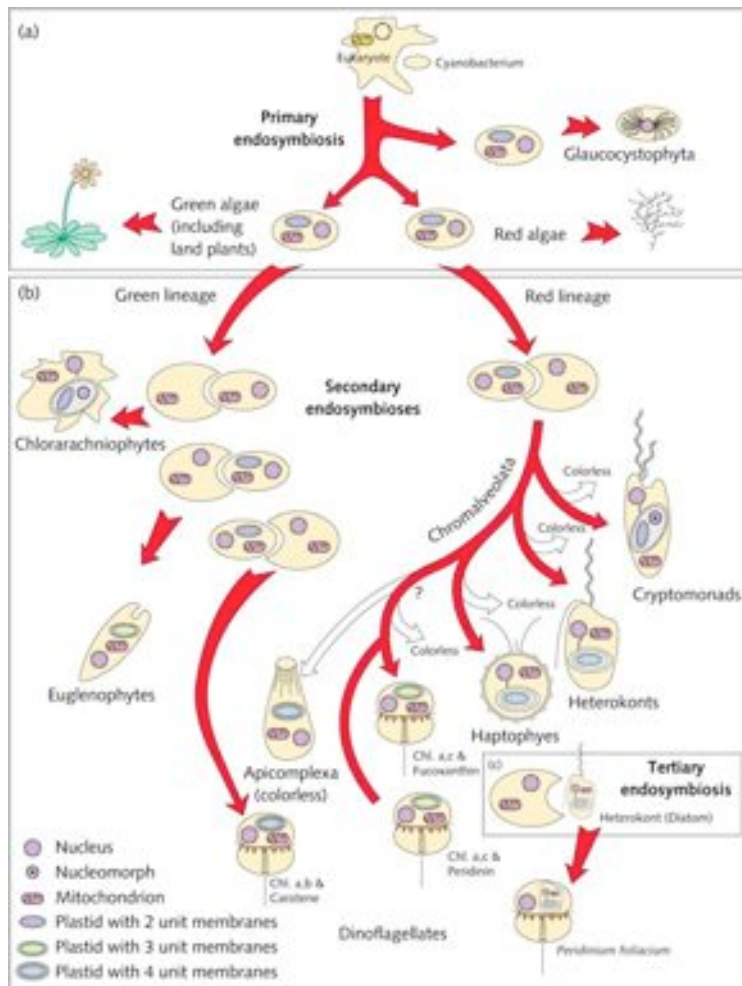
An example is the coevolution in interacting biological macromolecules, such as tRNAs and ribosomal proteins (Figure 11.20). Obviously, there has been reciprocal evolutionary change in both parties that led to a refined interplay between those entities.



**Figure 11.20** Ribosomal translation as an example for the the coevolution in interacting biological macromolecules

Other well-known examples are the ancient *endosymbioses* between prokaryotes and host cells that led to mitochondria and chloroplasts. On top of that, there have been further secondary and tertiary endosymbioses. The following steps can be traced back from cell biological and genetic analyses (Figure 11.21).

- $\alpha$ -proteobacterium  
-> mitochondria (1500-2000 Ma)
- cyanobacteria  
-> chloroplasts (several times, 800-1000 Ma)
- secondary and tertiary endosymbioses

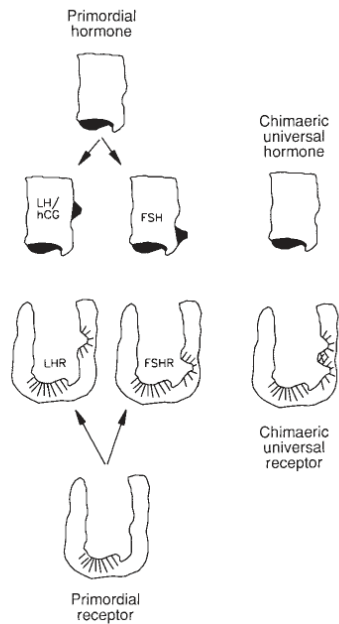


**Figure 11.21** Endosymbioses between prokaryotes and host cells that led to mitochondria and chloroplasts.

Coevolution of ligand-receptor pairs is an example where proteins are the coevolving entities. The example of luteinizing hormone (LH) / human chorionic gonadotropin (hCG) and follicle-stimulating hormone (FSH) coevolving with their receptors shows some principles:

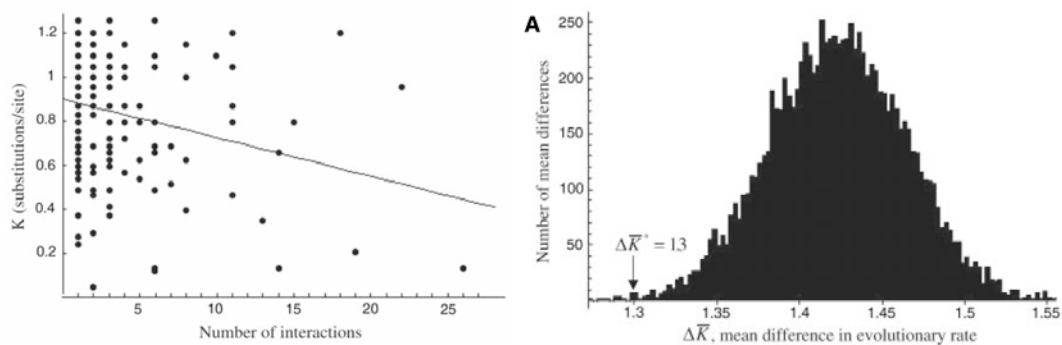
- Ligands such as hormones may have evolved from a common precursor and then diverged functionally.
- The receptors also seem to have arisen in this way.
- Distinct negative determinants restrict ligand-receptor interactions.
- Artificial chimaeric hormones and receptors lacking these determinants are universal.





**Figure 11.22** Model of coevolution of gonadotropin and gonadotropin receptor binding specificity.

Recent advances in proteomics and bioinformatics enable large-scale studies on the coevolution of interacting proteins. A recent high-throughput screen of yeast (*Saccharomyces cerevisiae*) proteins shows that proteins that interact a lot evolve more slowly, i.e. connectivity of well-conserved proteins in the network is negatively correlated with their rate of evolution (Figure 11.23).<sup>31</sup> This was because a greater proportion of the protein is directly involved in its function. Most importantly, interacting proteins evolve at similar rates. This implies that at sites important for interaction between proteins, evolutionary changes may occur largely by coevolution, in which substitutions in one protein result in selection pressure for reciprocal changes in interacting partners. Even though a completely different level was studied here, these results are comparable with cophylogenies on the level of macroevolution.



**Figure 11.23** Left: The relation between the number of protein-protein interactions ( $I$ ) in which a yeast protein participates and that protein's evolutionary rate, as estimated by the evolutionary distance ( $K$ ) to the protein's well-conserved ortholog in the nematode *C. elegans*. Right: The distribution of mean difference in evolutionary rate between yeast proteins randomly chosen from the list of all 411 interacting protein pairs in which both members had an ortholog in *C. elegans*. The mean difference in evolutionary rate between proteins that interact is indicated by an arrow.

<sup>31</sup> Fraser, H.B., *et al.* (2002) Evolutionary rate in the protein interaction network. *Science* 296, 750-752

### 11.5. Take home messages

- *Coevolution is reciprocal evolutionary change.*
- *Interactions can be classified as mutualism (+/+), commensalism (0/+) and antagonism (-/+).*
- *Although suggestive, full evidence is hard to obtain.*
- *Evidence of coevolution comes from experimental manipulation, cophylogenies and microevolution (local adaptation, coevolutionary cycles, SPE, virulence evolution, etc.).*
- *Coevolutionary interactions can change rapidly (geographic mosaic theory).*
- *Coevolution can occur on diverse levels, e.g. endosymbionts, ligands & receptors, proteins*

### 11.6. Literature

*Recommended textbooks for this chapter:*

Stearns, S.C. & Hoekstra, R. F. (2005) *Evolution: an introduction*. 2<sup>nd</sup> ed. Oxford University Press, Oxford.

Ridley, M. (2004) *Evolution*. 3<sup>rd</sup> ed. Blackwell, Oxford.

*Further reading:*

Lively, C.M., and Dybdahl, M.F. (2000) Parasite adaptation to locally common host genotypes. *Nature* 405, 679-681