

# Trematode behaviours and the perceptual worlds of parasites<sup>1</sup>

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**Abstract:** There is a great deal of empirical data and theoretical predictions on the patterns and processes of trematode behaviour, particularly in relation to host-finding activities by the free-living stages and site-finding migrations by the parasitic stages within their hosts. Ecological and evolutionary models of trematode life histories often make explicit assumptions about how these organisms must perceive and respond to signals in their worlds as they move from host to host and as they parasitize each host. Nevertheless, it is unclear how natural selection shapes the parasites' behavioural strategies. In addition, at each stage in their life cycle, trematodes are adorned with elaborate sensory organs and possess sophisticated neuromuscular systems, but it is not clear how they use these complex machinery to perceive their worlds. The purpose of this review is to address this question through insights gathered from a century of research on trematode behaviour. Core theoretical assumptions from modern animal behaviour are used to provide the context for this analysis; a key concept is that all animals have unique perceptual worlds that may be inferred from their behaviours. A critical idea is that all animals possess complex patterns of innate behaviour which can be released by extremely specific signals from the environment. The evidence suggests that trematode parasites live in ecologically predictable aquatic and internal host environments where they perceive only small subsets of the total information available from the environment. A general conclusion is that host finding in miracidia and cercaria, and site-finding by trematodes migrating within their definitive hosts, is accomplished through the release of innate patterns of behaviours which are adaptive within the context of conditions in the worm's environment. Examples from empirical studies are used to support the contention that, despite the apparent complexity of their free-living and parasitic environments, the perceptual worlds of trematodes are impoverished, and complex patterns of behaviour may be released by only a few signals in their environment.

**Résumé :** Il existe une grande quantité de données empiriques et de prédictions théoriques sur les structures et les processus des comportements des trématodes, particulièrement en ce qui a trait aux activités de recherche d'un hôte par les stades libres et aux migrations des formes parasites à la recherche d'un site dans leur hôte. Les modèles écologiques et évolutifs des cycles biologiques des trématodes sont souvent basés sur des présuppositions explicites sur comment ces organismes doivent percevoir les signaux de leur univers et comment ils y réagissent alors qu'ils se déplacent d'un hôte à l'autre et qu'ils parasitent chacun des hôtes. Néanmoins, il n'est pas clair comment la sélection naturelle module les stratégies comportementales des parasites. De plus, à chaque stade de leur cycle biologique, les trématodes possèdent des organes sensoriels élaborés et des systèmes neuromusculaires complexes, sans qu'on sache clairement comment ils utilisent ces mécanismes complexes pour percevoir leur univers. L'objectif de notre synthèse de la littérature est de répondre à cette question en utilisant les perspectives générées par un siècle de recherche sur le comportement des trématodes. Des présuppositions centrales tirées de l'étude moderne du comportement animal servent à fournir un contexte à notre analyse; un concept clé est que tous les animaux possèdent des univers de perceptions que l'on peut reconstruire à partir de leurs comportements. Une idée maîtresse est que tous les animaux possèdent des patterns complexes de comportements innés qui peuvent être déclenchés par des signaux extrêmement spécifiques en provenance de l'environnement. Il y a des indices qui font croire que les trématodes parasites vivent dans des habitats dont les conditions écologiques sont prévisibles, soit des environnements aquatiques, soit le milieu intérieur de leurs hôtes; les trématodes y perçoivent seulement de petits sous-ensembles de l'information disponible en provenance de l'environnement. Une conclusion générale est que la découverte des hôtes par les miracidies et les cercaires et la

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localisation des sites par les trématodes qui migrent à l'intérieur de leur hôte définitif se font par le déclenchement de comportements qui sont adaptatifs dans le contexte des conditions qui prévalent dans l'environnement du ver. Des exemples tirés d'études empiriques servent à appuyer l'assertion selon laquelle l'univers des perceptions des trématodes est relativement pauvre, malgré la complexité apparente de l'environnement de leurs stades libres et parasites. Un petit nombre de signaux en provenance de leur environnement suffisent à déclencher des patterns complexes de comportements.

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## Introduction

All animals are thought to live in species-specific perceptual worlds, and we intuitively understand that a bird, a dog, and a worm may each perceive their own worlds very differently. However, this was not so clear when the idea was first championed by the early pioneers in the study of behaviour. They argued that experimenters had to see the world the way their organisms saw the world before they could understand why their animals were behaving the way they were. They used some very elegant experiments to demonstrate how perception could be inferred from specific animal behaviours (von Uexküll 1934; Fraenkel and Gunn 1940; see later section). These early ideas provide the foundations for much of our current understanding of the ecology and evolution of animal behaviour, and this framework of species-specific perception is now being applied to a variety of parasite species from diverse taxa (Sukhdeo 1994; Lewis et al. 2002).

The study of parasite behaviour has lagged far behind other fields of behavioural study. For example, it was only 24 years ago that Saladin (1979) argued for "behavioral parasitology" to be recognized as a legitimate field of parasitological inquiry.

The umbrella of the medical perspective in parasitology, with its goal of improved immuno- and chemo-therapies, often constrains certain directions of research and may be partly to blame for our tardy entry into the field. However, a more probable reason was that parasitologists did not have the conceptual frameworks for asking questions or testing hypotheses on parasite behaviours. In the early literature, it was often abundantly clear from the method sections that authors had a good understanding of the adaptive value of certain parasite behaviours, but they still tended to report their observations simply as "wriggling" or "rapidly moving" worms, and the term "behaviour" was often used to refer to physiological interactions (e.g., expulsion behaviour of parasites in immune hosts) (Croll and Sukhdeo 1981; Sukhdeo and Mettrick 1987). Some of the earliest reports of parasite behaviour were studies on the attraction of the miracidia of *Fasciola hepatica* to lymnaeid snails (Thomas 1883; Leuckart 1894). However, most investigators did not recognize kinesis as orientation behaviours, and the field became very contentious (Ulmer 1971).

The rigorous study of parasite behaviour really began with the testing of an old hypothesis on host-finding behaviour that was borrowed from entomologists working with free-living parasitoid insects (the classic three step process; Salt 1935; Laing 1937; Wright 1959). This fueled an explosion of ideas and experiments on parasite host-finding behaviours during the 1960s and 1970s which validated the idea that parasites can "behave", and the majority of these studies were done with trematode miracidia and cercariae (MacInnis

1965, 1976; MacInnis et al. 1974; Ulmer 1971; Saladin 1979). Trematodes have dominated this field from the beginning, and even though the questions have changed dramatically, trematodes still remain at center stage. For example, an important recent discovery is that parasites, especially trematodes, can alter the behaviour of their hosts to make them more susceptible to predation by the next host. This idea that parasites can have profound effects on host competition and predation, the two major forces thought to be responsible for host community structure, is a serious challenge to current ecological models (Poulin 2001; Moore 2002).

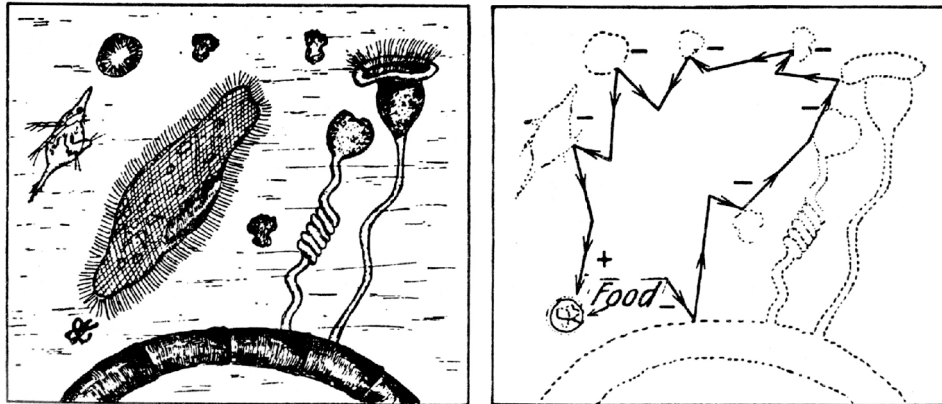
It is clear that powerful paradigms in ecology and evolutionary biology now dominate our thinking in parasite biology. Parasites play key roles in several important biological arenas including the evolution of sex (Lively 1987), mate choice (Hamilton and Zuk 1982), disease virulence, (Ewald 1995), and host population regulation (Hudson et al. 1998). There has been a proliferation of recent books and reviews on the ecology and evolution of host-parasite interactions (Sukhdeo 1994; Poulin 1998; Sorensen and Minchella 2001; Moore 2002; Lewis et al. 2002). Trematode ecology has been modeled at scales that range from local host-finding and transmission strategies (Combes et al. 1994, 2002) to larger scales of parasite community structure (Esch et al. 2001, 2002; Lafferty 2002). These models make implicit, and often explicit, assumptions about how trematodes must perceive and respond to signals in their worlds as they move from host to host and as they parasitize each host. In this review, we will examine what behavioural studies on trematodes tell us about their perception.

## The perceptual worlds of animals

Trematodes have complex species-specific and stage-specific behaviours, including host-finding, host-manipulation, and site-finding behaviours, that take them sequentially through free-living and parasitic environments. Each trematode stage in the life cycle has its own complex array of sensory structures, which are supported by sophisticated brains and neuromuscular apparatuses, but it is not all obvious how they use this equipment to perceive their worlds. Ethologists encountered similar problems when they first began to study the nature and evolution of animal behaviours, and the insights gained from these early studies may be useful to parasitologists seeking to understand parasite behaviours.

By 1973, when its proponents Konrad Lorenz, Niko Tinbergen, and Karl von Frisch were awarded the Nobel Prize, the idea of species-specific perceptual worlds in animals had become one of the core assumptions in modern animal behaviour. A crucial insight was that the mechanisms

**Fig. 1.** The perceptual world of *Paramecium* spp. (left panel). This organism responds negatively (–) to all stimuli in its environment (right panel), except to bacteria, its food source, where it responds positively (+) and moves forward to feed. (From von Uexküll 1934, reproduced with permission of International Universities Press © 1934.)



by which animals perceive the world are linked physiologically to the mechanisms by which the animal responds to the world (von Uexküll 1934; von Frisch 1950). For our purposes in understanding trematode behaviour, three important ideas have emerged from these studies: (i) there are species-specific differences in the sensory worlds of animals; (ii) many behaviours, including complex activities, are innate and require no learning; and (iii) there are several types of orientation behaviours in animals.

### (i) Sensory perception

Animals may perceive objects in space very differently from each other, and this can be a function of their sensory equipment. For example, humans possess one of the most sophisticated pair of eyes on the planet, and in terms of image quality and resolution, our visual space is qualitatively different from that of a fly with its compound eyes. In humans, our principal senses for localizing objects in space are touch and vision, and thus we speak of tactile and visual space. However, we do not think of ourselves as having an auditory space because our sense of hearing is far less accurate in localizing sounds in space (von Uexküll 1934). On the other hand, bats and owls have superb acoustic localization, and when we imagine their auditory space, it is in the same sense as we think of our visual space. Notably, total information from the environment is not always necessary for survival, and the types of signals and the quality of the signal reception will depend on the animal's needs. A frog may respond with the same feeding strike to both a passing dragonfly or a black dot moving in its visual space (Wehner 1981; Ingle 1983). Sea urchins only require photosensitive skins that allow them to point their spines defensively at fish in their environment (and to any large moving objects, including passing boats).

Even if animals were to have identical sensory equipment, each may recognize and respond to those signals that are important in their own biology and can be completely indifferent to all other signals in their environment (von Uexküll 1934; von Frisch 1950). For example, although *Paramecium* spp. are excellent foragers in their complex aquatic environment, they recognize and respond to only two signals, food and not-food. Their bacterial food source elicits a forward

movement and feeding activity, and everything else in the environment elicits an aversive reaction (backing up and turning) (Fig. 1). The classic example of the impoverishment of the perceptual worlds of some animals is seen in the host-finding behaviour of ticks. Although they live in a complex environment, ticks foraging for hosts recognize only three signals from the environment and have only three associated responses. Butyric acid, emitted by all mammals, induces the tick to drop from its perch; the mechanical stimulation of host fur induces crawling; and warmth (of host skin) induces the ticks to bore in for its meal (von Uexküll 1934).

The perceptual worlds of other animals may be far richer than those of *Paramecium* spp. or ticks, but it is clear that to understand their worlds, we must try to view each animal as the subject rather than the object of the environmental processes that affect its survival. Thus, when considering trematode behaviours, we must be attuned, both in perception and response, to the signals in the outside world that are most relevant to the animal's survival and reproduction.

### (ii) Innate behaviours

Lorenz and Tinbergen (1938, 1957) argued that complex behaviours such as imprinting in chicks or flight behaviour in birds were innate, did not require learning, and were released by specific signals in the environment. This is best illustrated by egg retrieval behaviour in the graylag goose, *Anser anser*. When the graylag goose sees an egg outside her nest, she goes through a stereotyped (exactly the same sequence every time) series of head movements, neck stretching, beak wobbling, and egg rolling to bring the egg back into the nest. The exciting discovery was that if the egg was removed in the middle of the pattern, the graylag goose would continue to carry out the full sequence of behaviours even though the egg was not physically there (Lorenz and Tinbergen 1938).

Released behaviours have now been reported from all animal phyla, and they all have in common the fact that the behaviours are released by very specific and extremely reliable signals from the environment (Alcock 1998; Krebs and Davies 1989). For example, the red dot on the beak of adult herring gulls (*Larus argentatus*) elicits a stereotyped pecking response in the chicks, or the red belly of male threespine

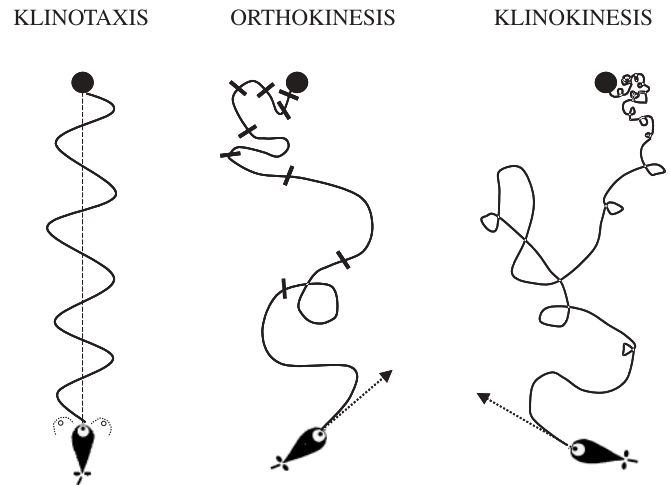
sticklebacks (*Gasterosteus aculeatus*) elicits attacks by other males (Pelkewijk and Tinbergen 1937; Tinbergen and Perdeck 1950). Interesting examples of released behaviours are seen during host finding by insect parasitoids. Parasitoids cannot detect new hosts the way bees might detect flowers because their hosts are under severe selection to avoid being found and eaten, and so they are difficult to detect directly (Vet et al. 2002). Thus, parasitoids respond to surrogates that reliably identify the host patch. For example, parasitoids of fruit flies (*Drosophila* spp.) aggregate around rotten fruit by responding to cues produced by decaying tissue. These cues release specific orientation behaviours that bring the parasitoids to the host patch, and these signals are reliable and the responses hard-wired because they have been honed over evolutionary time (Vet et al. 1990, 1995, 2002). The relationship between trematode parasites and their hosts have also been honed over evolutionary time, and one might imagine similar mechanisms of host finding.

### (iii) Orientation behaviours

There are two types of orientation responses (Frankel and Gunn 1940). Primary orientation is the positioning of the body in its normal stance (e.g., most fishes have a normal position in which the dorsal surface is uppermost and the longitudinal axis is horizontal). The fish may dart about during its daily business, but it always returns to this orientation. Secondary orientation occurs when the animals move towards (or away from) specific signals in the environment. Several animals, including passerines, salmon, honey bees, sea turtles, and monarch butterflies (*Danaus plexippus*) perform feats of navigation that continue to astound us. The mechanisms of many of these orientation responses are still not fully resolved and seem to require complex interactions at several levels including sensory, perceptual, endocrine, endogenous rhythms, and learning (Hasler 1960; Emlen 1969; Dyer and Brockmann 1996; Houck and Drickamer 1996). In contrast, it has long been known that even simple animals can orient towards particular features in the environment (Jennings 1906). Early ethologists studied these behaviours extensively, and Fraenkel and Gunn's (1940, 1961) book *The Orientation of Animals* codified the mechanisms of orientation in small animals on the basis of mechanical interpretations of their responses. Kinetic orientation mechanisms, where apparently random movements by the animal guides them towards the stimulus, are particularly important to parasitologists because they appear to be ubiquitous among parasites (MacInnis 1965; Croll 1970; Croll and Sukhdeo 1981; Sukhdeo and Mettrick 1987; Haas 1994a).

Orientation responses to a gradient of stimulus intensity can be divided into either directed (taxis) or undirected (kinesis) movements (Fraenkel and Gunn 1940) (see Fig. 2). In taxes, the animals move directly towards or away from the stimulus source. In kinesis, the animals change their behaviours in response to variations in the stimulus intensity. Miracidia and cercariae generally orient using klinokinesis, and in these responses the speed remains the same but the turning rate increases with intensity of stimulus. This response is probably better visualized in the response of a moth to an electric light bulb; as the moth gets closer and closer to the light (intensity increases), it is forced into ever tightening spirals (turning rate increases) that bring it bang-

**Fig. 2.** A diagrammatic representation of three basic types of orientation responses in small organisms. Taxes are directed responses (i.e., the organisms move in a straight line towards or away from the attractant). Kinesis are undirected movements. In orthokinesis, the organism slows down as they approach the attractant (the black bars on the tracks represent equal periods of time). In klinokinesis, the organism's turning rate increases as it approaches the attractant (redrawn from Sukhdeo and Mettrick 1987).



ing into the bulb. Orientation responses are innate behaviours that are released by specific signals in the environment, and thus are often used to identify biologically significant cues in the animal's world (Fraenkel and Gunn 1940).

### Trematode life cycles

The typical trematode life cycle has two intermediate hosts (Fig. 3). Monoecious adults occur almost exclusively in vertebrate definitive hosts and locate primarily in the gastrointestinal tract and its associated organs. Schistosomes are a notable exception because the adults of these trematodes are dioecious and live exclusively in the blood system. Trematode eggs are usually passed out with the host's faecal stream and hatch to release miracidia that almost always infect a molluscan first intermediate host. After penetrating the host, the miracidium transforms into an asexually reproducing sporocyst that may produce cercariae, daughter sporocysts, or rediae depending on the species. There are often consecutive generations of sporocysts or rediae prior to cercarial production, and in some species (family Philophthalmidae), the redial stage may develop within the miracidium and is released into the snail tissue after miracidial penetration. Cercariae emerge or are released from the molluscan hosts to infect and encyst in the second intermediate hosts, which includes a wide variety of invertebrates and vertebrates, or in the case of fasciolids, the cercariae will encyst on plant material. Transmission to the definitive host is almost always due to ingestion of the second intermediate host. Schistosomes have a derived two-host cycle and the cercariae directly penetrate and infect the definitive hosts. A few species are progenetic (e.g., in *Allocreadium* sp., the adults develop in diving beetles and caddisfly larvae).

Fig. 3. Typical life cycle of trematodes (redrawn and modified from Combes et al. 2002).

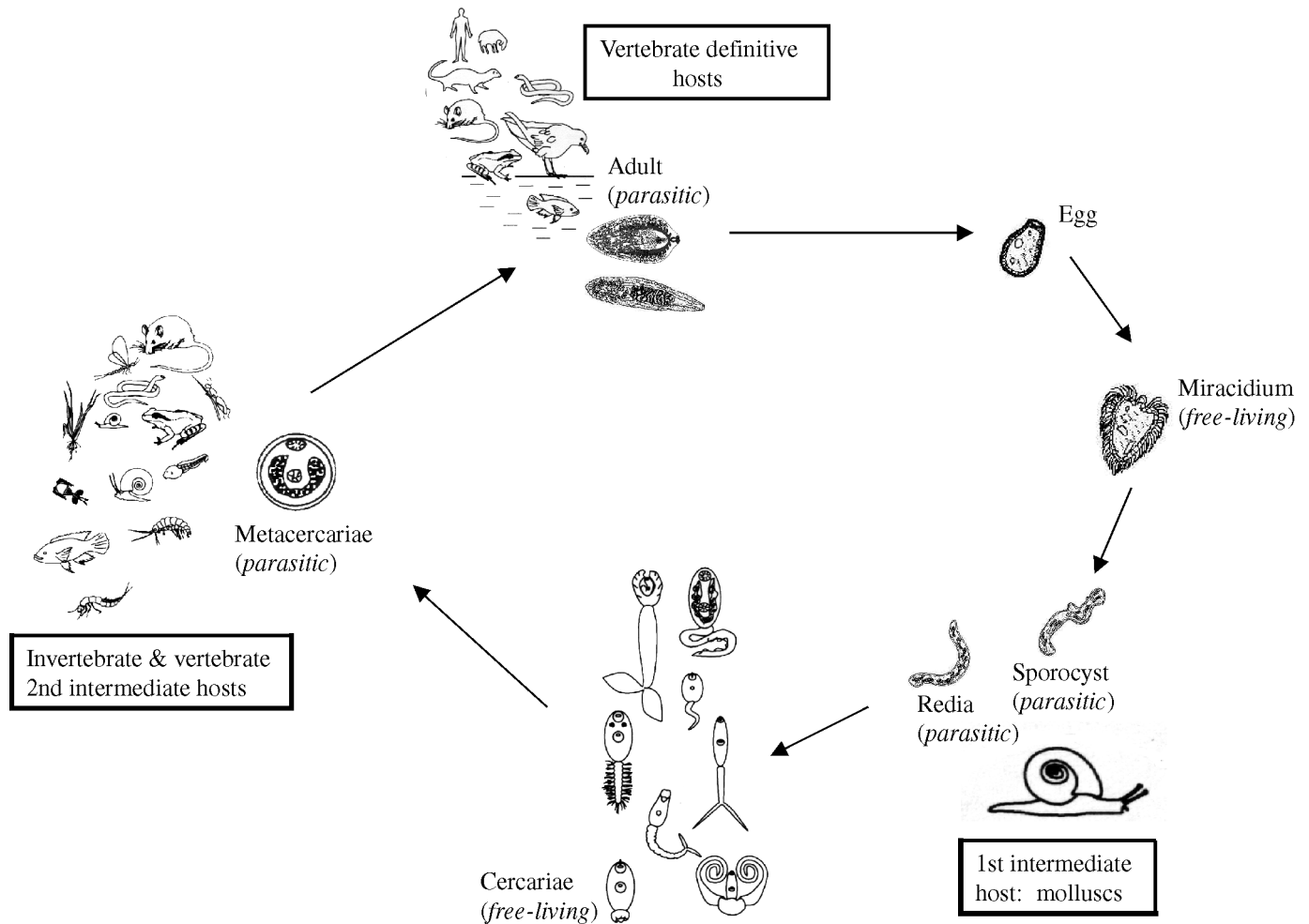


Figure 3 does not reflect the immense diversity of life styles among the 25 000 known trematode species and the many spectacular examples of structural and life cycle adaptations that challenge our curiosity. Nevertheless, there is probably more known about the genetics, physiology, evolution, biochemistry, phylogeny, ecology, immunology, and pathology of trematodes than for most other parasite groups. Thus, this review cannot be comprehensive and will focus primarily on studies on trematode behaviour that have been done during the last century to identify general patterns which have emerged.

## Free-living behaviours

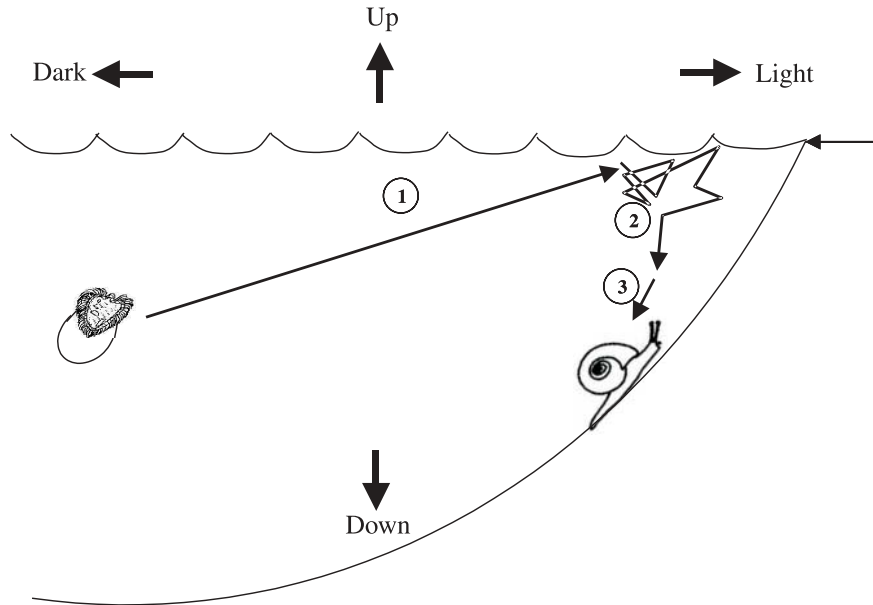
### Miracidia

The first step in miracidial host finding is hatching of the egg. Trematode miracidia develop within the egg, and most eggs have an operculum (window) through which the miracidium escapes. In many species, the miracidia are fully embryonated before they leave the host, while in others, several weeks in the external environment may be required. In species such as *Dicrocoelium dendriticum*, the eggs must be ingested by the snail host, and it is the physicochemical conditions in the snail's gut that triggers the hatching process (Ratcliffe 1968).

Egg production can be rhythmic; for example, in *Schistosoma haematobium*, peak periods of egg excretion in the urine of children occurred around noon when they tended to be in or near water (McMahon 1976). In most species, hatching occurs spontaneously in water, but light, osmotic pressure, and temperature appear to be important signals in several species (Smyth and Halton 1983). Hatching is generally inhibited by the conditions inside the definitive host, which prevents premature hatching, and it is triggered by environmental conditions preferred by its molluscan host. Thus, in schistosomes, the conditions within the host (blood, high osmotic pressure) and even within the faeces inhibit the hatching of the eggs (Garcia 1976; Kassim and Gilbertson 1976). The sudden shift from high (host or faeces) to low osmotic pressure (pond) appears to be the most important signal in the hatching of schistosome eggs (Kassim and Gilbertson 1976). For *Fasciola hepatica* eggs, light is important, and hatching is optimal in light at 16–20 °C. These conditions reflect the diurnal nature and temperature preferences of its snail host *Lymnae trunculata* (Rowan 1956; Mitterer 1975).

Once released from the egg, the imperative of the miracidium is to quickly locate and infect its snail because miracidia are non-feeding and rely on stored energy. Host finding is an active process that occurs in three distinct steps

**Fig. 4.** A diagrammatic representation of host-finding behaviours in trematode miracidia. The three-stage process consists of (1) dispersal to the host habitat in response to light and gravity, (2) random search in the host habitat, and (3) specific recognition and chemoattraction towards the molluscan host.



as first proposed by Wright (1959): (i) finding the host habitat, (ii) random search, and (iii) chemoattraction to the snail host. Wright's ideas were based on the studies of host finding by parasitoid insects (Salt 1935; Laing 1937). There have subsequently been many studies using parasitoids as biocontrol agents in agriculture and all parasitoid species studied seem to use some variation of this process (Askew 1971; Vet et al. 2002). This same basic strategy is used by miracidia, cercariae, and parasitoids and it may represent a convergence on the optimal solution to the problem of finding hosts.

#### (i) Location of the host habitat

Upon hatching, a specific behavioural pattern is spontaneously released in the miracidia and this takes it to the host habitat. During this first phase, which lasts from 1 to 3 h, miracidia tend to swim in fairly straight lines that are conducive to covering large distances quickly, but they are oblivious to their snail hosts (Campbell and Todd 1955; Ulmer 1971). This early blindness to the snail host caused much of the early controversy on whether miracidia were attracted to their hosts (Ulmer 1971). Investigators working with freshly hatched miracidia (Griffiths 1939; La Rue 1951; Chernin and Dunavan 1962) did not see any miracidial responses to the snail hosts, while those using "aged" miracidia found attraction to the snail host (Campbell 1961; MacInnis 1965; Shiff and Kriel 1970).

Almost invariably, the initial dispersal phase is controlled by responses to light and gravity (Ulmer 1971; MacInnis 1976; Sukhdeo and Mettrick 1987). Snails are known to have strong species-specific substrate preferences that occur in defined strata in freshwater ponds and lakes (Harman 1977; Turner 1996), and parasitologists generally accept that their habitats can be defined by only two axes: **light** (shallow) vs. **dark** (deep) and **up** vs. **down** (Fig. 4). The freshly

hatched miracidia of *F. hepatica* are strongly photopositive and their amphibious snail hosts *L. trunculata* are usually found near the surface at the edge of ponds (Wilson and Denison 1970a). The miracidia of the eyefluke *Philophthalmus lucknowensis* are geopositive and photonegative (move away from light), and this behaviour takes them to the habitat of their bottom dwelling snail host *Melanoides tuberculata* (Saxena 1981). The miracidia of *Philophthalmus gralli* are strongly geopositive (move in a downwards direction) and their snail hosts *Tarebria granifer* also live at the bottom of ponds (Keshavarz-Valian and Nollen 1980). Curiously, when these miracidia are placed in a magnetic field, they exhibited a north-seeking response that would also place them at the pond bottom in the northern hemisphere (Stabrowski and Nollen 1985). The mechanism by which this species detects magnetic fields is not known. Additional examples of miracidial geo- and photo-responses are seen in the responses of *Schistosoma mansoni* for its host *Biomphalaria glabrata*; *S. haematobium* for its host *Bulinus globosus*; and *Echinostoma caproni*, which responds exactly like *S. mansoni* and also uses the same host *B. glabrata* (Gerber 1952; Shiff 1969, 1974; Upatham 1972a, 1972b; Mason and Fripp 1976; Behrens and Nollen 1992).

The gravity receptors have not been identified, but light reception is most likely mediated by the eyespots on the miracidia. *Schistosoma douthitti* is photopositive with optimal light sensitivity in the blue-green spectrum (500–525 nm), and this is similar to most invertebrates with a dermal light sense (Steven 1963; Wright et al. 1972). The specific orientation mechanism to light is not clear. Mason and Fripp (1976) used a photographic technique that traced miracidial paths as a series of dots and concluded that light orientation was an orthokinesis because speed changed with stimulation intensity. However, a similar study on the miracidia of *F. hepatica* showed an increase in the rate of turning with in-

creases in light intensity, which Wilson and Denison (1970) concluded as being klinokinesis (Wilson and Denison 1970a, 1970b).

It is also not clear how the natural environment may interact with the geo- and photo-responses of miracidia. There are several factors including water flow, turbidity, natural obstacles, and predation that may affect the success of miracidial host finding (Prah and James 1977; Christensen 1980). For example, water flow may be of critical importance because flow rates >15 cm/s prevent miracidia of *S. haematobium* from finding *B. globosus* at the bottom of ponds, while flow rates as high as 105 cm/s do not affect the miracidia of *S. mansoni* from finding *B. glabrata* on the surface (Webbe 1966; Shiff 1969). Temperature can also alter the photoresponses of schistosomes (Takahashi et al. 1961; Shiff 1974; Mason and Fripp 1976). The distribution of snails in the pond is also sensitive to temperature, and the temperature effects on miracidial photo- and geo-responses are thought to produce parallel distributions of miracidia and snails (Shiff 1969, 1974).

#### (ii) *Random search for the host*

After 1–3 h, miracidia change their behaviour patterns and appear to spend their time searching for their host (MacInnis 1976; Ulmer 1971; Saladin 1979). The transition between dispersal and random search is not sharp and this phase has generally been ignored (Ulmer 1971; Saladin 1979). In miracidia of *S. mansoni*, there is a 15% decrease in speed and an increase in the turning rate (55–111°/s) as it enters into this search phase (Mason and Fripp 1976). A complicated statistical method applied to swimming speed, turning frequency, and turning angles concluded that during this phase the miracidia turned at random in a pattern which optimally explored three dimensional space (Plorin and Gilbertson 1981). Miracidia will continue this search pattern until they tire and die, unless they encounter their host.

#### (iii) *Specific attraction to the snail host*

It is now indisputable that “aged” miracidia can actively orient towards their snail hosts (MacInnis 1965, 1976; Ulmer 1971; Fried and Huffman 1996; Haberl et al. 2000). Early studies on miracidial chemoattraction were characterized by the design of sophisticated apparatuses, including chemotrometers, point inoculation methods, and four-armed choice chambers. These devices conclusively demonstrated that the miracidia preferred their specific snail host over any other choice (Campbell and Todd 1955; Chernin and Dunavan 1962; Etgers and Decker 1963; Plempel et al. 1966; Chernin 1970). However, the precise mechanism of the chemoattraction could not be determined in many of these systems and miracidial behaviour could often only be described as “excited” (Chernin 1970). Studies that analysed changes in speed and intensity suggested that the miracidia’s responses to the snail host were klinokineses (Wilson and Denison 1970a, 1970b; Shiff and Kriel 1970; Wright and Ronald 1972; Mason and Fripp 1976; Prechel and Nollen 1979; Roberts et al. 1979; Samuelson et al. 1984), but these were still regarded with some skepticism. The definitive evidence of klinokinesis came from a study on the behaviour of 5000 miracidia that were individually observed as they responded to gel pyramids impregnated with various chemicals

(MacInnis 1965). MacInnis (1965) created an objective assay based on behaviour that is still being used today (Sponholtz and Short 1976; Haas et al. 1991; Haberl et al. 2000). He classified miracidial behaviours into two broad categories: (1) contact with return, a positive klinokinesis involving 8 easily observed responses, and (2) contact without return, which was a negative or indifferent response. This method demonstrated unequivocally that the miracidia of *S. mansoni*, *S. douthitti*, and *F. hepatica* used klinokinesis to orient to chemicals secreted by their hosts (MacInnis 1965).

The chemoattractants are usually associated with snail mucous and tend to be reliable indicators of the host’s active space because they are by-products of the host’s normal physiological processes (MacInnis 1976). However, the precise nature of these signals has still not been satisfactorily resolved (Haas et al. 1991; Haberl et al. 2000). There have been several attempts to decompose snail-conditioned water into its component parts to isolate the active fraction associated with these responses. These studies indicate that a host of organic and inorganic compounds act as attractants for various species of miracidia; the organic and inorganic compounds include amino acids, fatty acids, sugars, MgCl<sub>2</sub>, Ca<sup>2+</sup>/Mg<sup>2+</sup> ratios, serotonin, reduced glutathione, HCl, H<sub>2</sub>SO<sub>4</sub>, ammonia, large glycoproteins, and snail mucus (MacInnis 1965, 1969; Shiff and Kriel 1970; Wilson and Denison 1970a, 1970b; Etges et al. 1975; Sponholtz and Short 1976; Stibbs et al. 1976; Nollen 1990; Behrens and Nollen 1992; Haas et al. 1995; Fried et al. 1997; Kalbe et al. 1997; Haberl et al. 2000). These results were often difficult to interpret, but most authors tried to find adaptive explanations for these responses. For example, miracidia of *S. mansoni* are attracted by specific Ca<sup>2+</sup>/Mg<sup>2+</sup> ratios, which are thought to be affected by the depletion of Ca<sup>2+</sup> in the vicinity of snails (Sponholtz and Short 1976; Stibbs et al. 1976). However, Haas et al. (1995) argued that miracidia should respond to macromolecules and not to small molecules so that they avoid incorrect responses to the numerous small molecular components of mud in the snail’s microhabitats. These authors reported that both *S. mansoni* and *S. haematobium* orient to large glycoprotein macromolecules from their snail hosts.

Interpretation is further complicated because miracidial responses to the snail can be generic or very species-specific, and it was not always clear why. In studies using snail-conditioned water from three snail species, an Egyptian strain of *S. mansoni* was significantly more attracted to *Biomphalaria alexandrina* than to *B. glabrata* or to *Lymnaea stagnalis*, whereas miracidia of a Brazilian strain of *S. mansoni* did not differentiate between these hosts and infected all equally (Haberl et al. 2000). The miracidia of the echinostome *E. caproni* also responded to these three hosts equally (Haberl et al. 2000), but other echinostomes can be very host-specific (e.g., *Hypoderaem conoidium* strongly prefers *Lymnaea peregae* over *Lymnaea corvus*; Toledo et al. 1999).

One unambiguous conclusion from these studies is that the best attractant is always the snail or snail-conditioned water (Chernin 1970; MacInnis 1976; Haberl et al. 2000). We know very little of the sense organs involved in these orientation responses and the notion that these receptors may be perceptually tuned to a gestalt of signals that identify the

host has not been generally considered in these reductionist studies.

### Cercariae

Cercariae are much more amenable to behavioural study than miracidia and there has been a lot more work on these trematode stages. The sheer volume of literature in this area is overwhelming, and the reader is referred to several reviews for additional information (Ulmer 1971; Cable 1972; MacInnis 1976; Saladin 1979; Smyth and Halton 1983; Haas 1992, 1994a, 1994b; Combes et al. 1994, 2002; Rea and Irwin 1994; Kearns 1998). In general, parasitologists accept that host finding by cercariae is strategically similar to that of host finding by miracidia and consists of the same three basic steps: (1) movement into the habitat, (2) energy efficient search, and (3) orientation and (or) attachment to the specific host (Haas 1994a).

The first step in circadian host finding is usually emergence from the snail host. Early investigators assumed that emergence depended on the physiology or behaviour of the snail host. Thus, while various physicochemical factors, including mechanical disturbance of the snails, temperature, light, humidity, and pH, could stimulate cercarial emergence in diverse species, it was thought that these effects were mediated through the snail (Kendall and McCullough 1951; Haas 1969; Asch 1972; Chapman 1974; Schmidt and Fried 1996). For example, light is a powerful stimulant and the exposure of snails to a light source is still the common method of stimulating cercarial emergence when collecting cercariae of *Schistosoma* spp. in the laboratory. Light was thought to act by increasing the snail's body temperature, which resulted in cercarial release (Asch 1972).

There are now classic experiments which demonstrate that cercarial emergence coincides with the times when the downstream hosts are most likely to be in the water (Combes and Théron 1977; Théron 1984; Combes et al. 1994). Thus, cercariae of *S. mansoni* tend to emerge around noon when humans are most likely to be in the water; the two peaks of emergence of *Schistosoma margrebowiei* at dawn and dusk correspond with visits to the watering places by its host antelopes and waterbucks (Raymond and Probert 1991), and *Schistosoma rodhaini*'s nocturnal emergence coincides with visits by its nocturnal rodent hosts (Combes et al. 1994). The adaptive value of some of these temporal patterns is not always obvious. In the same snail host *Goniobasis semicarinata*, the cercariae of *Proterometra edneyi* emerge during the early daylight when its visually feeding hosts (darters) are active, whereas those of *Proterometra macrostoma* emerge at night (Lewis et al. 1989). However, the night-emerging *P. macrostoma* is eaten by sunfish, which forage both night and day. These authors suggested that the nocturnal emergence of *P. macrostoma* might decrease predation by diurnal feeding non-hosts.

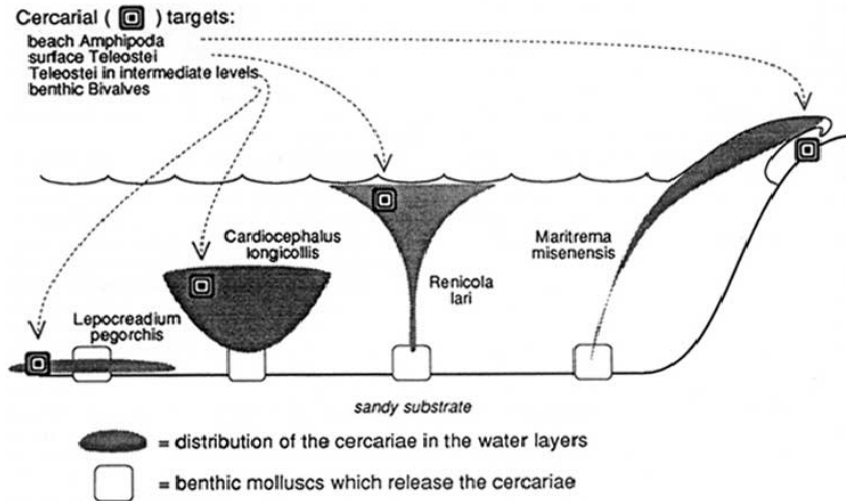
Experimental crosses of chronobiological strains with different emergence patterns support the idea that cercarial emergence is parasite-dependent and under genetic control (Théron 1989). In locations where *S. mansoni* infects both rats and humans, emergence occurs at night in the rat-adapted strain, but at noon in the human strain (Combes 1990). When *B. glabrata* was infected with two chrono-

biological strains of *S. mansoni*, one with an early shedding pattern and the other with a late shedding pattern, each strain kept its own cercarial emergence pattern without any interference between strains (Théron et al. 1977).

Emergence from the snail spontaneously releases innate and stereotyped patterns of behaviour in the cercaria that facilitate dispersal into their host's habitat. During this early phase, several species including *Diplostomum spathaceum*, *S. haematobium*, *E. caproni*, and *Cryptocotyle lingua* have high swimming activity until they reach their host habitats, whereupon they slow down (Haas 1992; Rea and Irwin 1992; Schmidt and Fried 1996). They tend to be oblivious to their hosts during this early phase. For example, *Echinoparyphium recurvatum* completely ignores its next host during this period of dispersal (Evans and Gordon 1983). In most species, cercarial orientation responses during this phase occur mainly to light and gravity (Kennedy 1979; Haas 1992, 1994a, 1994b; Combes et al. 1994, 2002; Loy et al. 2001). The most elegant demonstration of these dispersal responses comes from studies of trematode infections in a Mediterranean lagoon (Combes et al. 1994), and these data are reproduced in Fig. 5. These authors found that cercariae of different trematode species infecting bottom-dwelling molluscs responded very differently to light and gravity. *Cardiocephalus longicollis* emerges from the gastropod *Amiclinia corniculum* and then uses photopositive and geonegative responses to locate themselves halfway up the water column where their intermediate fish hosts swim. In contrast, the cercariae of *Lepocreadium pegorchis* have weak swimming activity and a strong geopositive response that keep them at the bottom where they are caught in the water current to be inhaled by several species of bivalves (Combes et al. 1994). The cercariae of *Maritrema misenensis* is released from *Centrium mediterraneum* and uses a photopositive response to swim up to the surface of the lagoon. Finding the host's habitat requires an extra step whereby they attach themselves to the underside of the surface film with their oral suckers and drift passively until wavelets wash them onto shore where their amphipod hosts *Orchestra gammarus* are found (Bartoli and Combes 1986).

Most cercariae possess paired eyespots of varying complexity that are used in their responses to light (Dönges 1964; Cable 1972). *Postdiplostomum cuticola* have eyespots and are sensitive to light, but *Apatemon* sp., which do not have photoreceptors, do not show any light sensitivity (Dönges 1964). However, the cercariae of *Microphallus similis* and several other microphaliid species that also do not possess eyespots have been shown to orient towards light, and it is thought that they use a dermal light sense (McCarthy et al. 2002). Studies on *Trichobilharzia ocellata* suggest that the light sensitivity of their photoreceptors work optimally in the blue-green spectrum (500 nm), which is similar to the light sensitivity of miracidia (Wright et al. 1972; Wright 1974). Cercarial responses to light and gravity are generally considered to be true taxes (Takahashi et al. 1961; Saladin 1979; Rea and Irwin 1992; Combes et al. 2002), although there have been few rigorous studies to identify the specific orientation mechanisms. The cercariae of *C. lingua* and *Cryptocotyle concavum* swim directly towards light in a helical path that alternately exposes each photoreceptor to

**Fig. 5.** Spatial dispersal of trematode cercariae in relation to the locations of their next host. (From Combes et al. 1994, reproduced with permission of Parasitology, Vol. 109, Suppl. 1994, © 1994 Cambridge University Press.)



the light source. In two light experiments modeled after Fraenkel and Gunn (1940), these cercariae oriented accurately between the two light sources, strongly suggesting that these cercariae use a tropotaxis (i.e., orient in a straight line perpendicular to the stimulus) (Rothschild 1939; Chapman and Wilson 1973; Chapman 1974). The cercariae of *T. ocellata* have a complex response to light whereby they can swim in a straight line away from the light source after it has been turned off (suggesting a primitive type of memory), and this is also a tropotaxis (van de Roemer and Haas 1984; Feiler and Haas 1988). In these cercariae, tail movements control directional movement. When the furcae are spread out, the cercariae move tail-first towards the light, and when the furcae are clapped together in line with the tail, the cercariae move away from the light (Feiler and Haas 1988).

The mechanism of cercarial locomotion is the tail, and there is a spectacular variety of shapes and sizes of tails that are thought to reflect the functional needs of each cercaria (Schell 1970). Cercariae that infect bottom-dwelling hosts tend to have short stumpy tails, or no tails, and they tend to crawl on bottom substrates. In *Philophthalmus* spp., the initial dispersal swimming phase lasts only about a minute, and the cercariae quickly sink to the bottom where they crawl along on their stumpy tails and eventually encyst (Nollen 1968). In cercariae that infect fish hosts, the tails may have structures and behaviours that often mimic their host's prey items (Combes 1980). The cercariae of *Azgia lucii* are very large and mimic mosquito larvae in size, colour, and behaviour, whereas the cercariae of *Gorgodera euzeti* have a conspicuous tail that looks like a wriggling worm, and both are very attractive to fish (Combes 1971; Combes et al. 1994). The cercariae of *Proterometra sagittaria* and *Proterometra hodgesiana* have huge tails (20–38 mm) which make lashing movements that attract their sunfish host (Prior and Uglem 1979). In some species, large numbers of small zygocercous (aggregating) cercariae get together into huge assemblages. *Cercariae caribea* and *Cercariae laramiensis* coalesce into flickering clusters or rosette formations that are very attractive to fish (Cable 1963; Martin 1968; Hendrickson and Kingston 1974; Beuret and Pearson 1994).

Swimming cercariae have tails of various lengths that may be forked, single, or bestudded with setae and other appendages (Kearns 1998). *Cercaria setifera* and *Opectonia bacillarius* have tufted tails that greatly enhance their speed; the rapid undulations of the tails sweep the tufts of setae backwards to push against the water to generate speeds of up to 13 m/h (Koeie 1975; Bartoli 1984). These tufted tails often accumulate debris and these species have an interesting behaviour where they stop swimming, reach around with their body to clasp the tail, and then they draw the tail through their body to clean it.

Many cercariae that infect mobile hosts (mostly fish) and including the schistosomes, sanguinicolid, opistorchids, and diplostomatids have furcocercous (forked) tails and have very similar patterns of swimming behaviours (Ferguson 1943; Erasmus 1958; Schell 1970; Haas et al. 1987; Haas 1994a). The classic description of these behaviours come from studies on *S. mansoni*. These cercariae initially disperse to the water surface in response to light, then enter into a search phase characterized by intermittent activity. They spend most of their time drifting down, generally using their tails as a parachute or a drag anchor, and at intermittent intervals, they swim upwards for a few seconds by rapid undulations of their tail and then sink again (Saladin 1980). The cercariae may also show resting postures where they attach to the water surface or solid materials. Intermittent behaviour is a mechanism used by many phyla, and its advantages lie in energy conservation and reducing predation (Kramer and McLaughlin 2001). During this phase, indirect cues signaling the presence of a potential host, such as turbulence or shadow effects, will trigger alterations of the behaviour pattern in ways that improve the chances of host contact. In *T. ocellata*, shadow responses initiate a long burst of swimming activity during which the cercariae quickly swim away from light and downwards, and this increases the probability of contact with the swimming feet of its duck hosts (Haas et al. 1990a). These swimming bursts stimulated by shadow responses are also seen in the cercariae of *D. spathaceum* and *Opisthorchis viverrini* that infect fish, and *Schistosoma spindale* that infect cattle (Haas et al. 1990a, 1990b). During swimming bursts, cercariae show a

strong tendency to attach onto any substrate that they encounter (Haas et al. 1990a, 1990b).

Characteristic cercarial swimming patterns have been documented in several trematode species and they cannot all be described here. These swimming behaviours exhibit many species-specific differences, but they all have in common the fact that the behaviour occurs in stereotyped and repeatable patterns (Graefe et al. 1967; Rees 1971; Chapman and Wilson 1973; Haas 1974, 1976; Whitfield et al. 1977; Prior and Uglem 1979; Bundy 1981; Coil 1984). A good example of the programmed nature of these behaviours is seen in the intermittent swimming behaviour of the furcocercous cercaria of *D. spathaceum* (Haas 1992). The swimming behaviour of these cercariae follows such a predictable program of activity that a simple model was developed, complete with light, dark, and turbulence as inputs, which explained all of the cercaria's swimming behaviours (Haas 1992). This is exciting because it profoundly illustrates the programmatic nature of the behaviour. Convincing evidence for the innate nature of cercarial swimming behaviour is seen in *P. macrostoma*, which is similar to the behaviour seen in *D. spathaceum*. In these cercariae, the complex swimming program is generated entirely by the tail, which will execute the program even if the cercarial body is removed (Prior and Uglem 1979; Uglem and Prior 1983). Neurophysiological recordings clearly demonstrate that all of the rhythmic activity of the cercaria's swimming behaviour is initiated within the tail and sensory feedback from the cercarial body is not required for the program (Prior and Uglem 1979). Similar findings that the tail can generate the complicated swimming patterns in the absence of the cercarial body has also been reported for *C. lingua* and *Himasthla secunda* (Chapman and Wilson 1973). It is clear from these studies that the tail is an autonomous locomotor organ that is specialized to produce the dispersal activity which brings the parasite to the next host. This has profound consequences on the way cercariae must perceive their worlds, and this topic is elaborated in a later section.

The next step in host location by cercariae is attachment and penetration. Several investigators have tried to demonstrate that the cercaria are attracted to their downstream host in the same way that miracidia are attracted to the snail host, but attraction was usually not seen, or the results were ambiguous (Faust and Meleney 1924; McCoy 1935; Neuhaus 1952; Cheng 1963; Smyth 1966). For cercariae that infect mobile hosts, chemoattraction has not been found, and these responses are probably unimportant because the hosts do not stay in one place long enough for these mechanisms to be efficient (Smyth 1966; Combes et al. 2002). In contrast, cercariae of *Echinostoma trivolvis*, *Echinostoma revolutum*, *Echinostoma echinatum*, and *Hypoderaeum conoideum*, which infect slowly moving snails, definitely do orient towards their hosts (Cheng 1963; Fried and King 1989; Hutterer et al. 1992; Haberl et al. 2000; Fried et al. 2002).

When cercaria get to their host, either by chance contact or via orientation responses, the direct contact with host skin releases attachment and penetration behaviours that can be quite complex and may involve distinct phases of attachment, creeping, and penetration (Haas et al. 1987; Haas et al. 1991; Haas 1994a, 1994b; Haberl et al. 2000). The signals for these attachment and penetration behaviours are still

not fully understood, but fatty acids and L-arginine are common signals used by cercariae invading mammals, birds, and fish (Haas 1974). The best triggers are always the host tissue, and despite the many attempts to decompose host tissue to find the specific signals in host recognition, attachment, and penetration, no clear picture of the host-recognition process has emerged (Wagner 1960; Stirewalt and Kruidener 1961; Stirewalt 1963, 1966; Thorson et al. 1968; Clegg 1969; Stirewalt and Uy 1969; Haberl and Haas 1992; Haas 1992, 1994a, 1994b; Haas et al. 1987; Haas et al. 2002).

## Parasitic behaviours

Parasitic behaviours in trematodes typically begin with penetration or ingestion of miracidium, cercaria, or metacercaria. In contrast to the immense volume of work on the free-living stages, there have been few experimental studies on the behaviour of parasitic stages, and thus, most of our inferences come from observational study. Much of the problem lies in the difficulty of observing and manipulating parasites in situ, because opening the host to see the worms can dramatically change the environmental conditions and the responses of the parasite.

### Within the snail

Parasitism usually begins with the penetration of the snail by the miracidia, but in many species infection may occur through ingestion by the snail, as in *D. dendriticum*. In penetrating miracidia, components of snail mucus stimulate attachment by adhesive secretions and (or) the sucker-like activity of the apical papillae; and after some intermittent lashing about, rotating, and the release of various cytolytic secretions, they suddenly slip into the snail (Smyth 1966; Wilson et al. 1971; Wright 1971; Wikel and Bogitsh 1974; LoVerde 1975). In some species the ciliated plates are discarded during penetration, whereas others penetrate fully before discarding the plates and transforming into sporocysts. Penetration often occurs in the foot of the snails, and although this is a nutrient-poor area, the sporocysts are non-mobile and tend to remain at this site. A frequent strategy is the production of mobile redial stages that migrate to richer tissue, often to the gonads. Alternately, some sporocysts of *Leucochloridium varia*, *Plagioporus sinitsini*, and *Echinoparyphium flexum* develop extensive branches that grow into the snail's tentacles, kidneys, or gut (Dobrovolny 1939; Ulmer 1952; Najarian 1954). In *Postharmostomum helices*, daughter sporocysts are transported to the hepatopancreas by long undulating branches of the mother sporocyst, and the daughters are expelled from the branches with forceful muscular contractions (Ulmer 1951). The sporocysts of *L. varia* and *Neoleucochloridium problematacum* send their tentacles into the antenna of their snail host *Succinea* spp., and these develop into brood sacs with bands of colour. In light, these brood sacs pulsate rhythmically to resemble insect larvae (Kagan 1952; Lewis 1974). These pulsating brood sacs are conspicuous at distances of 3 m for a human observer and may be even more conspicuous to their passerine hosts (Lewis 1974).

Migration to better sites in the snail is usually accomplished with rediae that locomote using muscular body contractions and ambulatory lappets that are shaped like wings.

Although the hepatopancreas and gonads appear to be the favorite organs to migrate towards, several rediae exhibit specific preferences that consistently bring them to the heart, buccal mass, albumen gland, kidneys, or rectum of their snail hosts (Rees 1934; Goodchild 1948; Alicata 1962; Cheng and Cooperman 1964; Heyneman 1966). Unlike sporocysts which absorb nutrients through their body walls, rediae have a mouth and muscular pharynx that allow them to feed on big chunks of tissue. However, they don't migrate directly through tissue to their sites, but instead seem to follow ducts and natural pathways (Cheng and Cooperman 1964; Probert and Erasmus 1965). For example, the redia of *P. gralli* migrates to the heart via the blood system of the snail host (Alicata 1962). Redial migrations may not always be directed towards getting better nutrients, and the rediae of *Ribeiroia guadaloupenensis* will first migrate to the snail's brain to stop the host's reproduction before these worms begin to feed on tissue (Nassi et al. 1979).

Several insights into the behaviour of rediae have come from studies of intraguild predation (predation on trematode competitors within the snail) and its effects on the structure of trematode communities (Esch et al. 2001, Lafferty 2002). In *Lymnae rubiginosa* infected with combinations of echinostomes, schistosomes, and strigeids, the echinostome rediae consistently ate the sporocysts of the other species (Lie et al. 1965). In subsequent studies of this intramolluscan warfare among trematodes, it was determined that a pecking order existed among more than 10 species coinfecting the same snail host (Wright 1971; Lim and Heyneman 1972; Kuris 1990). In general, bigger rediae were dominant over smaller rediae and rediae were dominant over sporocysts (Kuris 1990). The debate over whether these interactions are mediated through opportunistic browsing by the dominant rediae or whether the attacks are directed towards specific competitors has not been fully resolved (Sousa 1992; Esch and Fernandez 1994; Esch et al. 2001; Lafferty 2002). In similar-sized echinostome species, the dominant is the one that infects first and grows biggest first, supporting the opportunistic browsing hypothesis (Lie et al. 1965). On the other hand, rediae seldom feed on their own kind and tend to aggregate around subordinate trematodes, suggesting at least a kin recognition (Sousa 1992). Specific recognition of competitors would require investment in sensory structures and this would only be necessary if the worms encounter their competitors frequently. It is not yet clear if intramolluscan coinfections occur frequently enough in nature for these sensory structures to evolve and the debate on this issue still continues (Kuris and Lafferty 1994; Lafferty et al. 1994; Esch et al. 2001, 2002; Lafferty 2002).

#### Within the second intermediate host

Parasitism usually begins with penetration of the cercaria. Specific patterns of behaviours and the secretion of an assortment of glandular products facilitates this process (Smyth and Halton 1983; Haas et al. 1987; Haas 1992, 1994a; Haas et al. 2002). Some cercariae simply attach and immediately encyst on the host animal (or plant as in the case of *F. hepatica*), whereas others make migrations of varying difficulty through the host. The final site is often extremely specific to certain organs or tissue. The cercariae of the frog lung fluke, *Haematoloechus medioplexus*, encyst

nowhere else but in the brachial basket of the dragonfly prey (Krull 1931). The cercariae of *Megalodiscus temperatus* encysts only on dark-pigmented spots of frog skin (Krull and Price 1932). *Acanthatrium oregense* first encyst on the cuticle on the gills of the caddisfly larvae and uses this cyst as protection while the cercaria penetrates into the cuticle and encysts a second time (Burns 1961). Strigeoid cercariae of *Uvulifer ambloplitis* encyst just below the skin of the bluegill sunfish (*Lepomis macrochirus*) and create black spots that were long thought to increase predation by the host (Lemly and Esch 1984). However, this makes the fish more conspicuous to non-host predatory fish than to their avian hosts. It is now thought that these spots interfere with the schooling tendencies in infected killifish, *Fundulus diaphanus*, and these behaviours might make them more noticeable to piscivorous birds (Krause and Godin 1994).

There are numerous examples of cercariae migrating through the body and encysting in various organs where they often produce changes in host behaviour through mechanisms that are still not understood (Moore and Gotelli 1990; Poulin 1994; Moore 2002). The behaviours of dicrocoeliid and diplostomatid trematode are among the most studied of these manipulative relationships. When cercariae of *D. dendriticum* or *Dicrocoelium lanceatum*, produced in slime balls from infected snails, are ingested by their host ants *Formica pratensis* or *Formica polyctena*, several cercaria migrate from the abdominal cavity to the ant's brain where only one (occasionally two) will encyst in the subesophageal ganglion. After this occurs, the remaining cercaria in the brain return to the abdomen to rejoin those in the gaster where they all encyst (Schneider and Hohorst 1971). Infection results in a change in the behaviour in the infected ants. As night falls infected ants do not return to their nests with uninfected nestmates, but instead climb up vegetation and clamp themselves by their mandibles to the tips of the leaves where they remain until daylight when they unhook themselves, climb down, and rejoin their nestmates (Hohorst and Graefe 1961; Anokhin 1966; Schneider and Hohorst 1971). This behaviour is thought to increase the probability of infecting sheep grazing during the cooler hours around dawn and dusk. Ants infected with *Dicrocoelium hospes*, a parasite of African ungulates, assemble in motionless groups on plants where they remain for long periods of time and are even fed by uninfected nestmates (Romig et al. 1980). In *Brachylecithum mosquensis*, the migration of a single cercaria to the supraesophageal ganglion in carpenter ants, *Camponotus* sp., makes the ants obese and react with abnormal photopositive responses that brings them onto exposed rocks where their sluggish circling behaviour together with their great size makes them conspicuous to a human at 10 m, and they are presumably similarly conspicuous to their host, the robin (*Turdus migratorius*; Carney 1967, 1969).

The cercariae of *D. spathaceum* and *Diplostomum flexicaudatum* after penetrating the tails of fathead minnows, *Pimephales promelas*, can migrate to the eyes of the fish within 1–2 h (Ferguson 1943; Erasmus 1959; Ratanarat 1968). In the laboratory, guppies infected with this parasite were taken significantly more often than uninfected guppies by a predatory brook trout, *Salvelinus fontinalis* (Brassard et al. 1982). In a natural population of dace *Leuciscus leuciscus* on the Thames river, natural infections with *D. dendriticum*

did not cause much lens opacity, but those with heavy infections were often motionless or moving slowly at the water surface increasing their predation by the definitive host, the black-headed gull (*Larus ridibundus*; Crowden 1976; Crowden and Broom 1980; Owen et al. 1993). *Diplostomum baeri* migrate to the brain and locate in the choroid plexus of sticklebacks (Hoffman and Hoyme 1958), and *Diplostomum phoxini* migrates to the brains of the minnow *Phoxinus phoxinus* where they cause haemorrhage and swelling of the brain (Rees 1955, 1957). Cercariae of *Euhaplorchis californiensis* migrate to the brain of California killifish (*Fundulus parvipinnis*), and this drastically increases flashing, surfacing, contorting, shimmying, and jerking behaviours in the infected fish. These behaviour patterns increase its predation by a variety of piscivorous birds (Lafferty and Morris 1996).

In all of these associations, the manner in which the cercariae navigate and migrate through their hosts, and how they localize in specific areas of the fishes brain, is not really understood. The migration of *D. baeri* to the brain and *D. flexicaudatum* to the eye may occur via the blood stream (Ferguson 1943; Hoffman and Hoyme 1958; Betterton 1974). Whyte et al. (1991) suggested that the worms were also migrating through the lymphatics, but the speed of the migration has convinced some that the worms tunnel through connective tissue and muscle to get to their sites (Erasmus 1959; Ratanarat-Brockelman 1974).

#### Within the vertebrate host

Trematode infections of the definitive host almost invariably begin with the excystation of ingested metacercariae in the digestive tracts of their hosts. There have probably been more studies on excystment behaviour than for any other trematode behaviour, and numerous reviews have been written on this subject (Erasmus 1972; Lackie 1975; Smyth and Halton 1983; Sommerville and Rogers 1987; Sukhdeo and Mettrick 1987; Fried 1994; Rea and Irwin 1994). The signals that trigger excystation tend to be related to the physicochemical conditions within the host intestine, and these may include pH, temperature,  $P_{CO_2}$ , enzymes, secretions, and bile (Lackie 1975; Sommerville and Rogers 1987; Fried 1994). Excystment may occur through the passive digestion of thin cyst walls as with *Clonorchis sinensis* or it may require complex metacercarial behaviours that result in active breakout from thick cyst as in *F. hepatica* and *Martremia arenaria* (Dixon 1965, 1966; Irwin 1983; Sukhdeo and Mettrick 1986). Optimal conditions for excystment are generally found in the intestines of the definitive host; for example, *C. lingua*, a parasite of piscivorous birds, excysts best in the intestinal juice of gulls (Stunkard 1930; McDaniel 1966). Host temperature is often an important secondary signal, and in the bird parasites *Paraorchis acanthus* and *Posthodiplostomum minimum*, excystment is optimal at bird temperatures of 42 °C (Fried 1970; Fried and Roth 1974), and in *P. gralli*, which must quickly excyst in the throat of birds, this high temperature is the only stimulus required (Cheng and Thakur 1967).

The excystment behaviour of *F. hepatica* has been one of the most studied of these processes. There are two phases. A passive phase induced by conditions in the bovine rumen ( $CO_2$ , reducing conditions, 37 °C) that triggers an outpour-

ing of digestive enzymes from the caecum to soften the inner wall (Dixon 1966; Sukhdeo and Mettrick 1986). The metacercariae then remain quiescent until the cysts are transported into the small intestine where bile triggers the second phase, emergence. Video technology has shown that emergence is characterized by stereotyped patterns of rhythmic thrusting behaviours and sucker activity to disrupt the ventral plug through which the worm escapes (Sukhdeo and Mettrick 1986).

Bile is one of the most important triggers of excystment in trematode metacercaria. Of the more than 50 species from 19 families reviewed (Lackie 1975; Sommerville and Rogers 1987; Fried 1994), bile is the stimulus or co-stimulus of excystment in the vast majority. It is not clear why bile is a trigger for so many species, but this popularity suggests that it must be a very reliable indicator of arrival into the small intestine. Bile is a complex of substances made up of numerous components including mucin, proteins, bile pigments, conjugated and unconjugated bile salts, neutral lipids, phospholipids, and inorganic ions (Haselwood 1978). There have been several attempts to decompose bile to identify the specific signals. For example, a specific component of bile, glycocholic acid, stimulated optimal emergence (Sukhdeo and Mettrick 1986). Glycine-conjugated bile salts (typically found in herbivore bile) are always better triggers of emergence in *F. hepatica* than taurine-conjugated bile salts (typically found in carnivore bile) (Sukhdeo and Mettrick 1986, 1987).

After excystment, most trematode species remain as browsers in the intestine, but some make spectacular journeys to almost all organs in the vertebrate host. The paths taken and the navigation mechanisms are not known for most trematodes, but the migrating worms tend to follow defined paths using specific topological features (e.g., channels, ducts, and blood vessels during these migrations). For example, *Tamerlania* sp., a parasite of the kidneys of pigeons, consistently migrates to the kidneys via the ureters (Maldonado 1945). Trematode migrations were long thought to be chemoattractive responses to physiological cues produced by the final site, but despite hundreds of attempts with numerous species, no one has been able to demonstrate that orientation mechanisms are involved in any trematode migration (Ulmer 1971; Kemp and Devine 1982; Sukhdeo and Mettrick 1987; Sukhdeo and Sukhdeo 1994c, 2002). For example, it was thought that *C. sinensis* migrated to its final site in the liver by migrating up the bile duct in response to a gradient in bile (Faust and Khaw 1927), but when the bile duct was ligated, the worms were still able to migrate to the liver (Wykoff and Lepes 1957). We now know that normal migration in this parasite includes penetration of the intestine into the abdominal cavity and migration to the liver parenchyma (Sukhdeo and Mettrick 1987). A few species including *Philophthalmus* spp., *F. hepatica*, and *S. mansoni* have been the subject of really intensive studies on trematode migration in the definitive host.

*Philophthalmus* spp. are parasites of the orbital cavity of birds, although a few species live in the intestines. The metacercariae of *Philophthalmus megalurus* (triggered by host temperature) excyst quickly in the throat then quickly migrate through the nasolacrimal ducts to the orbital cavity within 3–5 h of excystment (West 1961; Danley 1973). Then

they enter the ducts of the Harderian gland where they spend some time maturing before they migrate to their adult sites on the nictating membranes (Danley 1973). When the ducts of Harderian gland were ligated, 87% of the metacercariae migrated to the eye with the intact Harderian system (Danley 1973). The migrations in *P. gralli* and *Philophthalmus hegeneri* are similar, but these species must first go deep into the conjunctival sac where they undergo their maturation before migrating to the adult sites on top or under the nictating membrane, respectively (Fried and Penner 1963; Colgan and Nollen 1977; Nollen and Murray 1978). When metacercariae of any of these three species are put into one eye, adults can often be recovered from the other eye in a process called intraocular migration. This generated a flurry of interesting experiments to understand this behaviour (Nollen and Kanev 1995). It appears that migration occurs in two distinct phases, each with its own suite of behaviours. The first step is migration of juveniles to their site of maturation and the second step is the migration of large juveniles (1.2 mm) to their adult sites. Intraocular migration only occurs during the second phase. It is not really a common phenomenon because most worms remain in the eye they were put into, but in large crowded infections (>50 metacercaria) up to 25% might cross over (Nollen 1983). Crossing over may occur when birds wash young worms down into the throat by an eye-flushing reflex and the worms can migrate back to either eye via the nasolacrimal ducts. Alternatively, the large juveniles might migrate down lacrimal ducts on one side, cross the nasal passageways, and migrate up the lacrimal ducts on the other side (Nollen and Murray 1978). This behaviour is stage-specific. Mature adult worms when placed in one eye will not migrate to the other (West 1961; Nollen 1968), and juvenile worms younger than 12 days will not make this migration either, at least not directly, but will first migrate to their maturation sites in the Harderian gland or the conjunctival sac (Nollen 1968, 1983; Nollen and Kanev 1995). The mechanism of orientation during these migrations are unknown. Studies in culture media suggest that the worms thrive on Harderian tissue, but attempts to find gradients and chemoattractive responses that explain migration *in vivo* have been unsuccessful (Danley 1973; Nollen and Kanev 1995). Young worms placed anywhere in the ductwork linking the two eyes will migrate to their maturation sites, and large juveniles placed anywhere in these ducts will migrate to the nictating membranes. The topology and architecture of the nasolacrimal ductwork is a fixed and constant feature in their hosts, and the worms might be using them as guideposts.

A similar two-stage pattern of behaviour is seen in *F. hepatica* during the migration from abdominal cavity to the liver. Metacercariae excyst in the intestine, penetrate the intestinal wall, and enter into the abdominal cavity. The worms do not take a direct route to the liver, but first go to the abdominal wall and then crawl along the wall to the liver (Sukhdeo et al. 1987). It was long thought that the worms in the abdominal cavity were attracted to the liver, but intensive efforts by many investigators could not find any worm orientation to the liver (Dawes and Hughes 1964; Doy and Hughes 1984; Sukhdeo et al. 1987). After much effort, Dawes (1963) concluded that the worms just wandered randomly, but he could not reconcile this conclusion with the

incredible success rate (40%–80%) of the tiny worms (250 µm) in finding the liver in hosts as large as sheep, *Ovis aries* (Montgomerie 1928; Doy and Hughes 1984). Dawes did not find chemoattraction because it is physically impossible to develop chemical gradients in the abdominal cavity. The turbulence generated by the constant writhing of the intestines would stir up all chemical gradients. In addition, the abdominal cavity is a closed system with no open end or sink, and thus chemical gradients would quickly become saturated. The indirect path to the liver via the abdominal wall does not require a response to gradients. Migration to the abdominal wall results from a specific crimping behaviour where the worms crawling in the viscera intermittently release their suckers and passively fall towards the floor of the abdominal wall. During this early migration phase, the worms are blind to the liver and wander off even if placed directly on the liver (Dawes and Hughes 1964). When the worms get to the abdominal wall, they use a creeping behaviour with a sliding motion that keep them adhered to the abdominal wall while they crawl to the liver (Sukhdeo et al. 1987). A similar pattern of leech-like creeping has been described in the frog parasite *Gorgoderina vitelliloba*, which must migrate down the wall of the intestine and up the ureter without getting dislodged by peristaltic activity (Mitchell 1973a, 1973b).

In *F. hepatica*, penetration usually occurs on the liver surface against the diaphragm and body wall, and the indirect migration route explains the mystery of why >80% of the worms penetrate the liver on the surface against the diaphragm of cattle (*Bos taurus*), rather than on the internal surfaces of the liver against the viscera (Doy and Hughes 1984). This indirect migration route is also used by other trematodes (e.g., *Paragonimus westermani*, a parasite of the lungs, has a similar migration path to the diaphragm where it penetrates through to the lungs). In a pattern similar to *F. hepatica*, after ingestion and excystment, the worms penetrate the intestines and enter into the abdominal cavity where they migrate to the abdominal wall. Here, they encyst for 6–10 days to mature, then emerge and proceed to the diaphragm, which sits directly on the liver (Yokogawa et al. 1962). For parasites crawling on the abdominal wall, the inside of the abdominal cavity is like the inside of an egg, and any direction taken will bring the worms to the liver/diaphragm junction. Thus, the predictable topologies of the abdominal wall and liver provide reliable routes for these worms.

In *F. hepatica*, the migration patterns appear to be released by signals contained within ingested tissue. Dawes (1963) felt that *F. hepatica* ate its way to the liver and, in an elegant study that combined worm behaviour with histology of the caeca, he demonstrated the sequential appearance of visceral tissue, abdominal wall muscle tissue, and then liver tissue in the caeca during migration. Worms feeding on visceral tissues exhibit crimping behaviours that take them to the body wall. Worms feeding on the abdominal wall tend to creep along the wall and worms feeding on liver tissue will enter the organ. These worms will make mistakes because they have to feed on tissue before they will recognize it. In *F. hepatica*, after the worms get to the liver/diaphragm junction, 25% of the worms penetrate accidentally into the diaphragm and leave holes as big as poppy seeds before turning

back and penetrating into the liver (Dawes and Hughes 1964). Similarly, in *P. westermani*, about 25% of the migrating worms first accidentally penetrate the liver before turning back and penetrate the diaphragm to get to the lungs (Yokogawa et al. 1960, 1962).

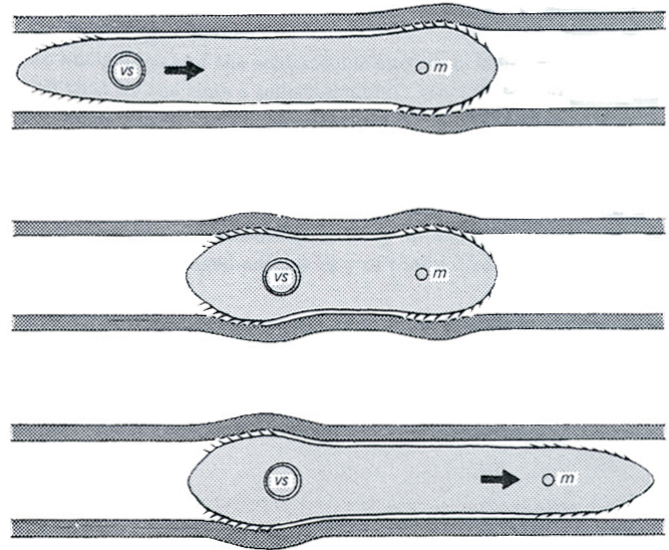
In *S. mansoni*, the migration to the liver also seems to occur in two distinct stages. In the first stage, cercariae penetrate into the dermis or via the hair follicles and into the venous system (Gordon and Griffiths 1951; Stirewalt and Dorsey 1974; Miller and Wilson 1978). The worms are then carried passively in the blood until they get trapped in the capillaries of the lung. Autoradiography of compressed tissue confirms that  $^{75}\text{Se}$ -labelled migrating worms (schistosomula) accumulate in the lungs (Wilson and Coulson 1986). The worms remain in the lungs for a minimum of 2 days while they mature and undergo significant structural changes in their bodies. The second stage begins with the subsequent migration from the lungs to the liver. This was thought to involve chemo-orientation responses and a direct migration through the diaphragm (Wilks 1967; Bruce et al. 1974), but in fact, the worms simply continue passively in the blood system to the liver (Yolles et al. 1949; Miller and Wilson 1978; van Marck and Gigasse 1978; Wheater and Wilson 1979; Wilson and Coulson 1989). The most significant discovery was that the worms in the lung greatly elongate their bodies. To do this they dissolve the fibrous interstitial layers that act as an exoskeleton on their bodies, and as they lengthen, their body diameter reduces from 25 to 8  $\mu\text{m}$ , which allows them to migrate through the capillaries (Miller and Wilson 1978; Wilson et al. 1978). During this stage, the worms express a characteristic stereotyped pattern of rhythmic cycles of contraction and extension (Fig. 6) (Wilson et al. 1978). The expression of spines only at the anterior and posterior ends of the body provide purchase on the wall of the capillaries, and the absence of spines in the midbody region minimizes friction between the worm surface and capillary epithelium. These rhythmic behaviours will even allow the worms to migrate in thin glass capillaries (Wilson et al. 1978).

After the worms migrate through the lungs, they are carried passively in the systemic circulation, and those entering the splanchnic arteries pass through the capillary bed in the gut using their new elongate bodies and inchworm behaviour, and then they are carried passively to the liver capillaries (Wilson and Coulson 1989). During this systemic migration, the worms do not develop further and will keep on circulating until they reach the liver. When they arrive in the liver capillaries, but in no other capillary bed, the worms begin to feed on tissue, their bodies shorten up, and their motility decreases significantly; these changes prevent them from accidentally passing through the liver (Wilson 1987). The specific signals from the liver that trigger the change in behaviour is not known (Wilson 1987), but as with *F. hepatica*, these cues seem to come from feeding on liver tissue.

### Trematode nervous systems

There have been a few detailed studies of the nervous system of trematodes (Ulmer 1953; Reisenger and Graak 1962; Dixon 1965; Rohde 1968a, 1968b; Silk and Spence 1969; Sukhdeo et al. 1988a, 1988b), but there has been little real

**Fig. 6.** The migration of *Schistosoma mansoni* through the capillaries of the lung. This migration is made possible by a metamorphosis that transforms the rotund worms into elongate and narrow bodies with terminal spines. A specific pattern of rhythmic inchworm behaviour is illustrated in the diagram. vs, ventral sucker; m, mouth. (From Crabtree and Wilson 1980, reproduced with permission of Parasitology, Vol. 81, © 1980 Cambridge University Press.)



progress since the first trematode nervous system was described from methylene blue preparations of *F. hepatica* (Bettendorf 1897). Trematode nervous systems show significant cephalization with distinct brains (cerebral ganglia) that send out eight longitudinal nerve cords (orthogonal pattern) which are connected by numerous transverse commissures (Bettendorf 1897; Bullock and Horridge 1965). Trematode nervous systems do not violate the fundamental neuron doctrine of distinct nerve cells (Silk and Spence 1969; Sukhdeo and Sukhdeo 1988; Sukhdeo et al. 1988a, 1988b). Ganglia are organized with a ring of neuron cell bodies surrounding a neuropile of interwoven axons and dendrites (Sukhdeo et al. 1988a), and within the neuropile, conventional synapses characterized by pre- and post-synaptic densities and well-defined synaptic clefts are numerous (Sukhdeo et al. 1988b). Studies on the morphology, architecture, sensory organs, and neuromuscular physiology support the idea that these nervous systems are equal to those of higher invertebrates, and similar function is often inferred (Sukhdeo and Mettrick 1987; Halton and Gustafsson 1996; Halton et al. 1997). Huge “giant” neurons that co-occur with specialized glial cells are found in the brains of *F. hepatica*, but in no other trematode brain (Sukhdeo et al. 1988b; Sukhdeo and Sukhdeo 1990), and similar structures called trophospongium have been found only in certain insects and molluscs (Bullock 1957; Hoyle et al. 1986). These giant neurons first appear in *F. hepatica* when immature worms begin feeding on liver tissue, and by the time the worms become adults, the giant neurons occupy up to 60% of the volume of the worm’s brain (Sukhdeo and Sukhdeo 1990, 1994a). The growth of these giant neurons coincides with the tremendous increase in the complexity and arborization of the worm’s

caeca, which in the adult worm might have >100 primary branches (Dawes 1963). Large diameter neurons are often used in the escape responses of invertebrates because conduction velocity increases with diameter in unmyelinated neurons (Bullock and Horridge 1965). Rapid nervous conduction of the giant neurons of *F. hepatica* is probably required to coordinate the complex peristaltic activity required to fill and empty the highly branched caeca of this parasite (Sukhdeo 1992; Sukhdeo and Sukhdeo 1994a).

Recent improvements in microscopic visualization combined with immunochemical staining of various neuroactive agents have led to an explosion of studies on the functional neuroanatomy of trematodes. Greater than 50 neurotransmitters and neuropeptides have been immunochemically localized in the nervous systems of miracidia, cercariae, and adults of various species (Smyth and Halton 1983; Gustafsson 1988; Halton and Gustafsson 1996; Halton et al. 1997; Zuwarski et al. 2001). However, apart from speculations based on the distribution of the stains in the nervous system, we are no closer to understanding function than we were 100 years ago. Interestingly, in these, and in most other studies on the nervous systems of trematodes, the immunolabelled neuroactive substances map directly onto locations in the central nervous systems of the parasites, but these stains almost never extend to connect with any sensory organs on the periphery ((Brownlee et al. 1995; Solis-Solo and de Jong-Brink 1994; McMichael-Phillips et al. 1996; Niewiadomska et al. 1996; Zurawski et al. 2001). For example, SALMFamide immunoreactivity in the cercariae of *S. mansoni* occur in the anterior ganglia and interconnecting commissures and in nerve tracts that extend anteriorly and posteriorly (dorsal and ventral) which terminate at the body/tail junction. In the tail only a pair of fine nerve fibers extend into each furca (Brownlee et al. 1995). Immunoreactivity to FMRFamide, vertebrate polypeptide P, peptide YY, and neuropeptide Y all show similar patterns as above, except there is no innervation to the tail (Solis-Soto and de Jong-Brink 1994, 1995; Skuce et al. 1990). In *Sanguinicola inermis*, serotonin and FMRFamide stainings were observed to extend to the tail but only serotonin extended to the furca (McMichael-Phillips et al. 1996).

Miracidia, cercariae, and adults of various trematode species display a large variety of sensory organs (including photoreceptors) that have been described from ultrastructural studies (Rohde 1968a, 1968b; Richard 1971; Short and Cartrett 1973; Short and Gagne 1975; Halton et al. 1997; Bogéa and Caira 2001). These sensory structures and their locations on the trematodes' bodies are consistent and are used as taxonomic characters (Richard 1971; Bogéa and Caira 2001). Numerous criteria including the presence or absence of cilia or ciliary sheaths, number of cilia, length of cilia, the presence of basal bodies, and the presence of ciliary rootlets have been used to distinguish the receptors (Halton et al. 1997; Bogéa 1998; Gustafsson 1998). However, although we can infer some functions from structure and location (e.g., chemo- vs. mechano-reception), we can only guess at the real functions of most of these receptors and the nature of the signals that stimulate them. The major obstacle is that we have not been able to develop a preparation which allows consistent microelectrode penetration of trematode nerve cells (Pax and Bennet 1991, 1992; Sukhdeo 1992a).

The acoelomate bodies of trematodes prevent the isolation of individual nerve cells, and without electrophysiological access to cells, we are unable to test neuron function rigorously.

There is a common assumption that trematode nervous systems control the organism's behaviour, but this is not always so. For example, the brains of *F. hepatica* seem to be primarily involved in the worm's digestive function (Sukhdeo 1992a). The brain is also important in feeding behaviour of the free-living flatworm *Notoplana acticola*. This worm uses the margins of its body to perform a complicated pattern of grasping and transporting its shrimp prey back and into its posterior mouth. When the entire brain is surgically extirpated, this complex feeding behaviour is unaffected, but the worms' satiation responses are altered and they continue to feed themselves as long as they are presented with shrimp (Koopowitz 1974, 1982). In the rat tapeworm *Hymenolepis diminuta*, removal of the scolex (containing the entire brain) did not affect the complicated rhythmic behaviours of the strobila, and these brainless worms were even able to orient up heat gradients as quickly as the intact control worms (Sukhdeo and Kerr 1992; Sukhdeo 1992b). Tapeworm brains seem to be used primarily in coordinating the complex egg-assembly operation of the strobila, and not with locomotion (Sukhdeo 1992a). In the cercariae of *P. macrostoma*, the brain resides within the cercarial body, but locomotion is provided entirely by the tail without any input from the brain (Uglem and Prior 1983). This sort of decentralized control of locomotion is not novel, and there are many cnidarians (jellyfish) that have very complex behaviours, but possess no brains and only limited nerve nets (Mackie and Meech 2000). The interrelationships between locomotion, sensory reception, and central nervous function are not clear, and without information provided by intracellular recordings, there will be little advancement in our understanding of the physiological nature of these functions in trematodes.

## The perceptual worlds of trematodes

In this discussion, we will argue that trematode parasites live in ecologically predictable aquatic and internal environments where they perceive only small subsets of the total information available from the environment. Thus, the perceptual worlds of trematodes at all stages can be considered impoverished. For example, a key observation is that complex host-finding behaviours of cercariae can reside entirely within the cercarial tail, and these patterns proceed even in the absence of the cercarial body and brain. The brain is the seat of perceptual integration, and because it is disconnected during host finding, the cercaria seem to not be perceptually aware of its environment even as the tail responds to light and turbulence. Indeed, the first unambiguous environmental signals that cercariae recognize are direct cues emanating from their specific hosts, and these release attachment and penetration behaviours. All behaviours prior to this event are part of host-finding programs that are spontaneously released during cercarial emergence. It can thus be argued that the perceptual worlds of cercariae consists solely of the host signals which trigger attachment and penetration.

The consistency of these host-finding responses in any given cercarial species suggests that these behaviour patterns

are innate programs. The minimal amounts of neuronal circuitry in cercarial tails suggest that programs are probably hard-wired and fashioned by selective pressure during host finding. The great diversity in the shapes, sizes, and behaviours of cercarial tails, each specialized for very narrow niches, provides indirect evidence of the selective forces acting on these organs. In this regard, it is important to recognize that cercaria searching for their hosts actually do not search for the hosts directly. Instead, they search for the space and time where the probability of meeting their specific host is highest (Combes et al. 1994, 2002). This is an important distinction that is crucial to our understanding of trematode behaviour because it explains why many parasites are indifferent to their own hosts, especially if the signals are presented out of context. In addition, the parasites need only respond to a few general cues (e.g., light and gravity) that define their host's space accurately in time and space, because the advantage of general responses is that they allow for rapid adaptation to new situations (Combes et al. 2002).

Host-finding behaviours in cercariae are classic released behaviours (i.e., complex patterns released by key environmental signals) and these types of behaviour tend to evolve under very predictable conditions (Sukhdeo and Sukhdeo 1994c, 2002; Sukhdeo et al. 2002). Studies of our waterways overwhelmingly support the idea that a predictable relationship occurs between conditions in streams and ponds, and the types of animals and plants that will occur (Magdych 1984; Karr 1991, 1999; Chessman 1995; Barbour et al. 1999). Ponds and streams are often viewed as isolated microcosms with consistent patterns of flora and fauna, and host animals such as snails and fishes occupy very specific and predictable habitats (Harman 1977; Turner 1996). Under these predictable conditions, plasticity in host-finding behaviours may *not* be important for cercarial host finding. In contrast, in terrestrial environments where visual cues add extra complexity, hard-wired behaviours are often not sufficient for successful host finding by parasitoids. In parasitoids, hard-wired host-finding strategies can be modified by experience, and more than 25 species of parasitoids have demonstrated the ability to learn (Turlings et al. 1993; Vet et al. 2002). For example, *Cotesia glomerata*, a parasite of caterpillars of the genus *Pieris*, learn to fly to the host-plant species that carries the most hosts (Geervliet et al. 1998a, 1998b). Trematodes likely do not have the capacity for learning because their nervous systems are not as sophisticated as those in higher invertebrates. In addition, the repeated exposures to their hosts that are required for learning do not occur with trematodes since they generally infect the first host they find.

The strategy of using innate released behaviours also characterizes host finding by miracidia and the migrations of trematodes within their hosts. As with cercariae, the blindness of these stages to their hosts or their final sites during the first behaviour programs provides key evidence for the releaser nature of these programs. For trematodes migrating within their hosts, it has long been recognized that habitats within the host have well-defined structures which are repeated across all individual hosts. Tissue and organs are physicochemically and topologically consistent and always occur in the same positions relative to each other, and the

entire body is interlaced with ducts and blood vessels organized in anatomically predictable patterns (Sukhdeo 1990; Sukhdeo and Sukhdeo 1994c). Thus, it is likely that the behavioural strategies of the migrating worms will also take advantage of the host's predictability. Szidat (1969) thought that diplostomatids migrating to the fish eye possessed an "engram" or a specific memory of the migration path that was fixed over the course of evolution. However, such a mechanism would require that the parasites be continuously aware of their surroundings so that they could compare their location with the engram. Instead, migrating trematodes express innate behaviour programs that bring them to their next site, and these often rely on topological features of the host (e.g., intraocular ducts or systemic blood vessels) as guideposts or highways for their migration. In the three well-studied examples of trematode migration in *Phlophthalmus* spp., *F. hepatica*, and *S. mansoni*, the very complex migrations through their hosts can be explained by just two patterns of behaviour. As with miracidia and cercariae, these behaviours are programmed to get them to the time and space where encountering their final site is highest. Thus, migrations in the host often include distinct developmental stages (time) that coincide with their arrival at the final site (space) (Sukhdeo and Sukhdeo 2002).

A general conclusion of this paper is that host finding in miracidia and cercaria, and site finding by trematodes migrating within their definitive hosts, is accomplished through the release of innate patterns of behaviours which are adaptive within the context of the conditions in the worm's environment. The focus of this review has been on host finding and migration, but there are many other behaviours that potentially exist in trematode repertoires such as behaviours related to feeding, mating, and site fidelity that have not been extensively investigated. For example, during feeding, the adults of *F. hepatica* attach to the mucosa of the bile duct by their ventral suckers (Sukhdeo et al. 1988c). When the host eats, the gastrointestinal hormone cholecystokinin-pancreozymin (CCK-PZ) is released, which stimulates the bile duct to contract and expel its contents including the worms. However, *F. hepatica* is a blood feeder with access to gastrointestinal hormones, and CCK-PZ stimulates increased contractions of the ventral suckers to hold the trematode fast during the expulsive bile duct activity (Sukhdeo and Sukhdeo 1989). In this case, the endocrine system of the hosts provides reliable signals and it is part of the perceptual world of the blood-feeding adult *F. hepatica*. Other trematodes may perceive their environments in ways that we have yet to imagine.

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