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# Filaria zoogeography in Africa: ecology, competitive exclusion, and public health relevance

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**Six species of filariae infect humans in sub-Saharan Africa. We hypothesise that these nematodes are able to polyparasitise human hosts by having successfully, through competitive exclusion, adapted to distinct niches. Despite inhabiting the same host, adult stages reside in different tissue sites. Microfilariae of some species exhibit temporal separation by reaching peak levels in the blood at specific times of day. Spatial and temporal distributions in microfilaria location are exploited by the vector feeding-behaviour whereas adult survival is enhanced by occupying exclusive 'ecological' niches of the body. We present specific examples to demonstrate this concept, which is not only important from the biological aspect but important in the context of elimination programmes.**

## Competitive exclusion in parasite biology

Competitive exclusion or Gause's Law [1,2] states that two species competing for the same resources cannot stably coexist if other ecological factors are constant. When one species has even the slightest advantage over another, then one will dominate in the long term, or one of the competitors will adapt via a behavioural shift towards a different ecological niche. Gause's Law is considered valid only if ecological factors are constant. There have been several studies on competitive exclusion in parasite–host systems. Examples include cestodes in the gut of sticklebacks [2]; the gills of eels and carp infected with Monogenean parasites [3,4]; human schistosome–host interactions in Central Africa [5]; the tick-borne blood parasites *Babesia*, *Theileria*, and *Anaplasma* in livestock in Morocco [6]; and *Taenia* parasites in Southeast Asia [6]. Moll and Brown [7] discuss competition and coexistence in species with multiple life-history stages using amphibian models. However, they do not discuss examples of parasites in their theoretical models. They define complex life cycles as life histories that experience an 'abrupt shift in habitat and diet that may be accompanied by a change in morphology', precisely that experienced by parasites transmitted by vectors. Much of the earlier work on between-species competition focused on *Drosophila*, *Tribolium*, or amphibians as the basis of the development of theoretical models of interspecies competition [7].

There has been longstanding recognition of the potential for competition between parasites within their hosts. Several reviews on multi- or polyparasitism have been published in both the geographic context [8] and in the context of the relationship with the immune system [9,10] as well as with parasite adaptation to within-host competition using malaria and bacteria as models. More theoretical approaches to the topic have been discussed [11], which present the phenomenon in the context of community ecology, focusing on patterns of parasite abundance across

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## Glossary

**Concomitant immunity:** the phenomenon in which active infection with an organism prevents additional infections by the same species of organism. In filariasis, active infection with adult filarial worms confers partial protection against further infections by invading L3 larvae.
**Dahomey Gap:** refers to the portion of the Guinean forest–savanna mosaic that extends all the way to the coast in Benin, Togo, and Ghana, thus separating the forest zone that covers much of the south of the region into two separate parts. The forest region west of the gap is called the Upper Guinean forests or Guinean forest zone, and the portion east of the gap is called the Lower Guinean forests, Lower Guinean–Congolian forests, or Congolian forest zone.
**Loiasis:** the disease caused by infection with the parasite *Loa loa.* The disease is also known as Calabar swelling or tropical eyeworm because adult worms migrate across the eye. Tabanid flies of the genus *Chrysops* transmit the infection.
**Microstratification overlap mapping (MOM):** the concept of defining the overlapping distribution of infections or co-endemicity in a particular geographic area at a finer level of spatial resolution than mapping of infections has previously achieved or been considered necessary.
**Onchocerciasis:** the disease, also known as river blindness, caused by the parasite *Onchocerca volvulus* and transmitted to humans by blackflies of the genus *Simulium*, which bite in the proximity of fast-flowing water sources where larval forms are found.
**Periodicity:** the phenomenon seen in filarial parasites when the parasites are found in the blood in peak numbers at particular times of the 24 h cycle.
**Prevalence:** in epidemiology, is the proportion of a population found to have a condition (typically a disease or a risk factor such as smoking or seat-belt use). It is arrived at by comparing the number of people found to have the condition with the total number of people studied, and is usually expressed as a fraction, as a percentage, or as the number of cases per 10 000 or 100 000 people.
**Stage L3 larvae:** the larvae that develop in an insect vector of filaria parasites, are deposited on the skin of the host at the time of the bite, and give rise to infection in the human host.
**Sympatric distribution:** when two species or populations are considered to exist in the same geographic area and thus regularly encounter one another.
**Zoogeography:** the discipline that is concerned with the geographic distribution (present and past) of animal species.

host populations rather than on mechanisms which underpin the interactions in hosts. This approach was based on laboratory models of parasite–environment interactions and the genetic basis of parasite and host interactions [12]. The application of these concepts to parasites of health, social, and economic importance, and the consequences of such interspecific competition on epidemiology, geographic distribution, and hence control or elimination, have received limited attention.

## Competitive exclusion in filarial parasites: the biological context

In this review the example of filarial parasites in Africa is discussed. Six filarial parasites can infect people in sub-Saharan Africa, including *Wuchereria bancrofti*, *Onchocerca volvulus*, *Loa loa*, *Mansonella perstans*, *Mansonella streptocerca*, and *Dracunculus medinensis*. *W. bancrofti* and *O. volvulus* are responsible for significant morbidity, causing elephantiasis and river blindness, respectively [13,14]. *L. loa* is not such a major pathogen, and presents as tropical eyeworm or Calabar swelling, whereas *M. perstans* and *M. streptocerca*, found in the blood and skin of humans, respectively, can cause mild symptoms, but typically are not thought to cause severe disease [15,16]. *D. medinensis* (Guinea worm) is close to eradication, but is still endemic in South Sudan where over 99% of 542 total cases were reported in 2012, as well as in Chad, Ethiopia, and Mali [17].

Notably, Guinea worm, although traditionally considered to be a filarial worm, is not classified in the same order as the other filariae. Although all are in the phylum Nematoda and class Secernentea, *Dracunculus* is in the order Camallanida and family Dracunculidae. Other filariae are in the order Spirurida: family Onchocercidae. In addition, *Dracunculus* have copepods (water fleas) as intermediate hosts. The dipteran vectors of the five filarial parasites are from diverse taxonomic family groups: *W. bancrofti* is transmitted by species of the mosquito genera *Anopheles* and *Culex* (family Culicidae); *O. volvulus* by *Simulium* species (blackflies; family Simuliidae); and *L. loa* by *Chrysops* species (deer or tabanid flies; family Tabanidae), whereas *M. perstans* and *M. streptocerca* are transmitted by midges of the genus *Culicoides* (family Ceratopogonidae) [18].

We discuss here the ecology and zoogeography (see Glossary) of filarial infections in Africa and hypothesise that competitive exclusion enables sympatric distribution of these parasites in both human and insect hosts, and influences their geographical distribution and biology of transmission. Knowledge of their zoogeography is of operational importance to target mass drug administration to endemic communities during elimination programmes. Lymphatic filariasis and onchocerciasis programmes need to be implemented in areas co-endemic for loiasis where there are attendant risks of serious adverse events associated with the use of ivermectin in individuals with high *L. loa* parasitaemias [19–21].

## The human host as the ecosystem and niche separation

We propose that the five sympatric, insect-transmitted filarial parasites in human and insect hosts inhabit an ecosystem, the human host, where it is important that each stage of the parasite has developed a strategy to ensure its survival in humans while at the same time maximising the opportunity for transmission. The different species of filarial worms occupy habitats within the human host ecosystem, being located in various tissues as adults, and in the blood or the skin as niche environments for microfilaria larvae, and hence accessible to insect vectors. Distribution within these habitats reduces potential competition, as does the temporal positioning achieved by microfilarial periodicity or the location of microfilariae in either the skin or blood.

This, in part, reduces competition but also enables a species to exploit the unique resources available in that niche. Parasites are not unlike other species although they are rarely considered through an ecological lens of environment, habitat, and niche within a host. Humans provide the ecosystem services for parasite survival, nutritional resources, and opportunities for transmission. This is particularly relevant for human filarial infections because there are no animal reservoirs to perpetuate transmission in the absence of humans; hence the need for such specific in-host partitioning. The ability to adapt to the immune responses of the human host, and for microfilarial larvae to locate to the blood or skin, is consonant with the biting habits and feeding behaviour of susceptible vectors vital for transmission. Reducing the risk of competition for transmission has been dependent on the strategy of this partitioning allied to the exploitation of periodicity. Filarial parasites, human hosts, and insect vectors, particularly feeding habits and the time of peak biting and how they obtain blood, represent a complex mix of organism interactions. The only filaria species where there is a potential animal reservoir is the simian form of *Loa*, but it appears not to infect humans and is transmitted by canopy-dwelling *Chrysops* vectors, which occupy separate parts of the forest with a different periodicity to human *Loa*, and humans are rarely exposed to this parasite [22,23].

The vectors that transmit filaria parasites, however, also differ in feeding methods for instance, pool feeders (blackflies) that create a lesion under the skin before a blood meal and capillary feeding by mosquitoes [18,24,25]. The distribution of potential competitor species within any ecosystem is important in terms of survival, competition for nutritional resources, and avoidance of predators, and in parasites the combating the immune response of the host and ensuring transmission. We highlight here the operation of ecological phenomena such as interspecific–intergeneric competition and the partitioning of filarial distributions of both adult worms and microfilarial larvae in the human body. The location of adult filaria worms is either the skin, lymphatics, or sub-cutaneous tissues, whereas the microfilariae are in blood or skin, with the temporal partitioning (periodicity) of blood-dwelling microfilariae being attuned to the biting habits of the vector (Table 1).

## Periodicity and competitive exclusion

The phenomenon of periodicity of microfilariae is well documented [22,26,27]. Periodicity in the peripheral blood historically has been attributed to maximising transmission efficiency, the peak of biting being attuned and

**Table 1. Species of human filarial parasites of Africa and their periodicity in humans and main vector species[a,b]**

| Human and vector species characteristics | *Onchocerca volvulus* | *Loa loa* | *Mansonella perstans* | *Mansonella streptocerca* | *Wuchereria bancrofti* |
|---|---|---|---|---|---|
| Adult worm in human | Subcutaneous tissues and skin nodules | Subcutaneous migration through skin and eye (Calabar swelling) | Peritoneal cavity | Subcutaneous tissues of upper chest and shoulders | Lymphatics |
| Microfilaria in human | Skin | Blood | Blood | Skin | Blood |
| Microfilaria periodicity | None | Diurnal | None | None | Nocturnal |
| Vector species and periodicity | *Simulium spp*  Day | *Chrysops spp*  Day | *Culicoides spp*  Crepuscular | *Culicoides spp*  Crepuscular | *Anopheles/ Culex spp*  Night |

[a]Excluding *Dracunculus medinensis* and Guinea worm.

[b]Image sources: http://www.cdc.gov; http://www.vectorbase.org; http://www.stanford.eud/group/parasites/.

synchronised with the timing of the appearance of the microfilariae in the blood at the highest densities to facilitate transmission. In the case of lymphatic filariasis, the host–parasite relationships between the filariae and vectors have been well studied. There are five genera of mosquitoes that act as vectors (*Anopheles*, *Aedes*, *Culex, Mansonia*, and *Ochlerotatus*) in different regions across the distribution of *W. bancrofti* and *Brugia malayi*, and *B. timori* (in Asia), but there are locally specific vector–parasite associations with varied transmission capacities [28]; for example, *Culex* mosquitoes in West Africa seem to be refractory to *W. bancrofti* [29–31]. Earlier laboratory studies demonstrate the genetics of susceptibility of different mosquito species to filarial infection, as well as pathology caused when filarial parasites enter the gut of some vectors [32]. The capacity of humans to act as hosts of all human filarial parasites is clear, but the likelihood that all parasites infect any one individual seems to be driven by other factors including vector abundance, the local ecology, and human behaviour. Hence, the determination of filaria parasite distribution in humans and vectors will be dependent on several factors.

Table 1 demonstrates partitioning of filariae in the human body of adult worms, and there is also partitioning of microfilarial niches: *O. volvulus* in the skin, *L. loa* in the blood during the day, and *W. bancrofti* in the blood at night. Although periodicity is usually attributed to the biting patterns of the respective vectors, an alternative hypothesis might be that, in the case of *W. bancrofti* and *L. loa*, there is a need for niche separation to enhance the efficiency of transmission and reduce competition. This separation would avoid the potential interactions of two microfilarial species entering an inappropriate vector in the same blood meal causing potentially lethal damage as non-compatible microfilariae enter the vector mid-gut. In Central Africa and parts of West Africa the five filarial species are regarded as co-endemic [16,25,33–39], although more refined mapping may show that there is less overlap than previously thought, with environmental factors playing a key role in determining vector distributions and transmission potential [21].

## Geographical distribution and ecological distinction

It is probably rare that any one individual is infected simultaneously with all filariae, although in parts of the Democratic Republic of Congo (DRC) this might be possible, as described in the Region of Bandundu [40]. An extensive literature review [25] provides details of historic surveys undertaken in the DRC; these studies have been re-examined in relation to existing control and elimination programmes [21], highlighting significant differences between *W. bancrofti*, *L. loa*, and *O. volvulus* at a micro-level through micro-stratification overlap mapping (MOM), a prerequisite to determining the finer levels of parasite distribution. Recent surveys and detailed maps confirm the contrasting epidemiology of *L. loa* and *O. volvulus* [41] and, as far as the DRC is concerned, a distinct absence of *W. bancrofti* has been noted in areas where *L. loa* is highly endemic [42–45]. Likewise, this inverse relationship can be extended to tropical forest regions of Gabon and Cameroon where the prevalence of *W. bancrofti* and *O. volvulus* is relatively low [46–49]. Interestingly, however, high *L. loa* and *M. perstans* prevalences are found to coexist geographically [48–50], suggesting that particular filariae are sympatric. Their success and ability to coexist in the same area may be attributed to vector periodicity and host partitioning: for instance, the diurnal *Chrysops* spp. of *L. loa*, primarily a subcutaneous disease compared to the crepuscular *Culicoides* of *M. perstans*, which predominantly affects the peritoneal cavity (Table 1).

An epidemiological study in Cameroon investigated the prevalence and intensity of infections of three filariae, *L. loa*, *O. volvulus*, and *M. perstans*, in a sample of 1458 individuals [51]. The three species displayed varying degrees of coinfection with a low prevalence of co-occurrence between *L. loa* and *O. volvulus* and the *L. loa–M. perstans* pair, in contrast to a high prevalence of co-occurrence of *O. volvulus* and *M. perstans*. Studies on polyparasitism included observations of *L. loa*, *M. perstans*, and *M. streptocerca* in rainforest villages in the DRC and concluded that there was a statistically significant association between the three species, especially the numbers of microfilariae of *M. perstans* and *M. streptocerca* [52,53]. The

reason for these geographic distributions as opposed to the individual differences is difficult to explain. Examination of the distribution of *M. streptocerca* in the DRC showed a wide distribution in the northeastern, central, and western regions of the Congo River basin area, but not in the mountainous southeast and extreme east where altitudes were high and ecologically distinct [39].

Although no continental African map for *M. streptocerca* is available, the recent distribution maps of the other four filarial species indicate that throughout West Africa, west of Benin, *W. bancrofti*, *O. volvulus*, and *M. perstans* are broadly co-endemic, whereas east of Benin to the borders of Uganda and the DRC all species are co-endemic and sympatric to varying degrees [34–38]. These differing distributions could be related to the well-defined Dahomey Gap in West Africa, which is a savanna corridor that extends to the Atlantic coast in Benin, Togo, and Ghana, and separates the West African rainforest into two regions. The forest regions to the west and east of the Dahomey Gap are the Guinea and Congo forest zones, respectively [54]. The rainforest habitats of western Ghana, Cote d'Ivoire, and Liberia seem capable of providing habitats for *Chrysops* vectors. However, although there is some historical evidence of loiasis in these countries [55,56], recent reports are lacking, which may be related to land-use changes, deforestation, migration, urbanisation, and/or expansion of agriculture. The geographical limits of *L. loa* and its main vectors appear to be bound by significant ecological and topographical features, including the Dahomey Gap and the Niger Delta (west), Sahelian and Sudanian savanna (north) [54], the Congo River Basin (central) [57], and high elevations >1000 m (east and south) including the Albertine Rift of the Great Rift Valley in the east [58], which is adjacent to some of the highest mountains in Africa (Figure 1). Although *Chrysops* spp. have been found in East Africa in the Eastern Arc Mountains, there is no evidence of loiasis, and this may be related to the different species found in this region [59].

These broad scale geographical differences provide clues to the ecological drivers associated with overlapping and distinct filarial distributions, and need to be understood in detail. Here we present Uganda as an example, where *L. loa* prevalence is low or absent despite high endemicity in the neighbouring DRC [38,60] (Figure 2). This could be related to the mountain range dividing the two countries, the relatively high elevations, and lack of dense tropical rainforest suitable for *Chrysops* in Uganda [54,56]. The distribution of *O. volvulus* is also limited and most prominent in the northern Nile River region [61], which contrasts to recent distribution maps showing *W. bancrofti* in the northeast region [62] and *M. perstans* in the southern region of the country [15]. Interestingly, *M. perstans* has also been associated with a condition known as Kampala, or Ugandan eyeworm, which occurs when worms invade the eye and which can be confused with other filarial diseases such *L. loa* [60]. Although limited data exist for *M. streptocerca*, the first study carried out in the 1990s in Bundibugyo district found high *M. streptocerca* prevalence in an area not endemic for onchocerciasis [16,63]. The authors emphasise the importance of differential diagnosis because each disease appeared to affect separate parts of the body, with *M. streptocerca* affecting the shoulders, chest, and arms with no ocular involvement, compared to onchocerciasis, which involved the eyes, pelvic region, and skin on the leg.

## Immunity

One of the interesting biological phenomena of filarial infections is that high numbers of adult worms do not typically infect an individual. For example, studies in Liberia showed that individuals harboured a mean of 16 adult *O. volvulus* worms even though vector biting-frequencies and rates of vector infection revealed that individuals were exposed to over 700 infective larvae per year [64]. Because *O. volvulus* worms usually live more than 10 years, the level of infection observed was markedly below

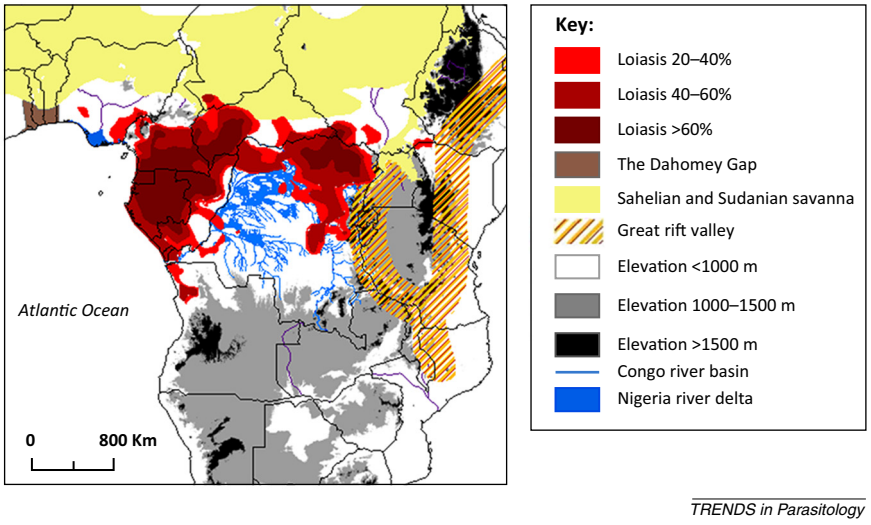


**Figure 1.** Loiasis distribution in relation to large ecological characteristics in Africa. This map shows the large geographical expanse of high-risk loiasis across Central Africa (in red), which is surrounded by distinct ecological and topographical features including the Dahomey Gap (brown), Niger Delta (blue), Sahelian and Sudanian savannah (yellow), Congo River Basin (blue), and high elevations (grey).

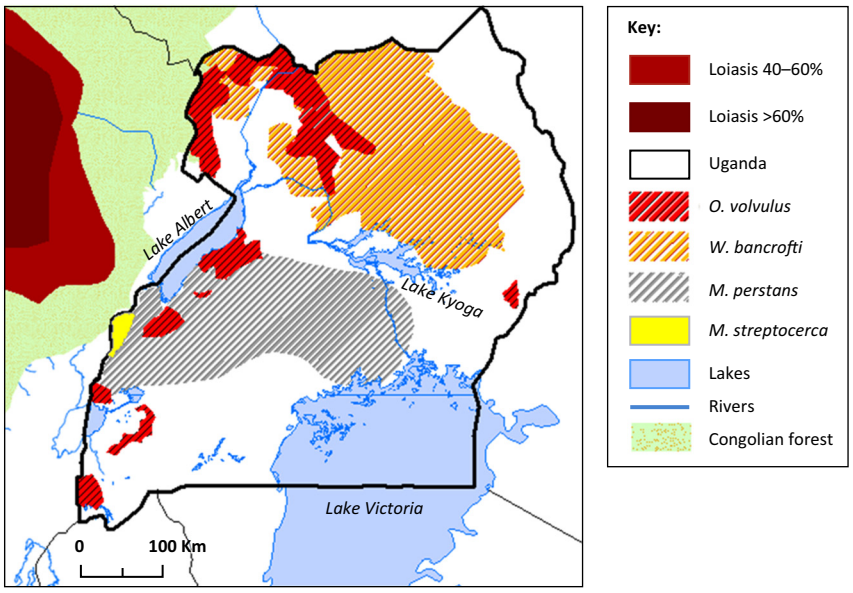


**Figure 2**. Distinct distributions of human filaria in Uganda. This map shows the differing geographical distributions of the filariae within one country, and highlights the lack of geographical overlap between them.

that expected based on parasite exposure. Concomitant immunity, the concept that active infection with adult worms protects against infectious stages of worms, may provide an explanation as to why individuals do not have a high parasite burden in areas of high endemicity. Numerous animal studies have shown that secondary filarial infections given during a time of active infection with adult worms are less successful than primary infections [65–68]. The presence of adult filarial worms is shown to inhibit invasion with infectious L3 stage larvae by greater than 50%, and that this effect occurs even after surgical implantation of a single adult female worm [69]. By preventing the development of lethal worm burdens, concomitant immunity is beneficial to both the parasite and the host [64]. To date, the mechanism by which concomitant immunity occurs in filariasis remains a mystery.

Although prevailing views argue that adult worms induce an immune response that selectively targets infectious stage L3 larvae [69–71], the data for this are scant. An alternative possibility is that adult worms may release a factor that inhibits the development of L3 worms. Similarly, the absence of zoonotic sources of infection in human filariasis adds additional pressure in terms of the need for survival and niche partitioning in the human host species [22]. The relationship between simian *Loa* parasites has not been investigated recently, and given the importance of *Loa* as an impediment to the expansion of onchocerciasis and lymphatic filariasis elimination programmes in Central Africa this needs further study. For example, does transmission of simian *Loa* to humans provide any degree of protection from *L. loa* infection and reduce the likelihood of such individuals developing high *L. loa* parasitaemias?

## Concluding remarks and significance for elimination and control

We hypothesise here that the epidemiology and distribution of filaria parasites in Africa is driven by complex interactions in the human host. These interactions enable co-infection with different genera and species through the phenomenon of competitive exclusion, which reduces the likelihood of competition for resources by the distribution of adult and microfilaria larvae into separate niches in the human host through spatial and temporal segregation. Periodicity of microfilariae has been postulated to enhance transmission by the synchronisation of peak abundance of microfilariae in the blood. An additional explanation is that vector survival is enhanced by avoiding ingestion of microfilariae and thereby preventing vector mortality. Programmes to eliminate onchocerciasis and lymphatic filariasis based on preventive chemotherapy with either ivermectin for onchocerciasis, or a combination of ivermectin and albendazole for lymphatic filariasis, are ongoing in Africa. These programmes are based on mapping of prevalences of infection using rapid assessment methodologies [38,41], although the problem of severe adverse events when people with high parasitaemias of *L. loa* are treated with ivermectin has been an impediment to the expansion of these programmes in some countries of Central Africa [19,20]. This paper highlights that, although there is some degree of co-endemicity, there are also areas where competitive exclusion reduces this co-endemicity, and geographic distribution of the parasites is also determined by geographic and ecological barriers.

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