Mathematical modelling of diffusion & transmission of livestock diseases mechanically transmitted by biting insects; acquired knowledge and perspectives

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Introduction

Biting insects such as tabanids and stomoxes, are present in all kinds of landscapes. Their geographical distribution and spatio-temporal dynamic are strongly driven by landscape fragmentations and by climate and its changes. In humans and animals, especially in livestock, these insects can act as mechanical vectors of a number of pathogens. Performing as small syringes, they can take infected blood from a host (0.05-10 nanoliters) and, following an interrupted bloodmeal, inoculate this blood into nearby host a few seconds or minutes later, at short distance [1]. In experimental works conducted under laboratory conditions, mechanical transmission of pathogens has been demonstrated by artificially interrupted feeding of insects on an infected host followed by resumption of the meal on another host. Although the ability for mechanical transmission of a number of potential vectors, like stomoxyines (*Stomoxys nigra*, *S. taeniatus*, *Haematobosca squalida*) and tabanids (*Tabanus importunus*, *Cryptotylus unicolor* and *Tabanus nebulosus*) has been demonstrated [2-7], their role in the epidemiology of trypanosomoses was still controversial since some authors considered that these experiments did not reflect the reality and that field observations were inadequate to prove mechanical transmission.

Trypanosome as a model was ideal: a single parasite can infect a host and be seen and counted by microscopic observation. A series of experiment was thus carried out in Burkina Faso; it clearly demonstrated the potential of mechanical transmission of African trypanosomes by tabanids [8-10] as briefly reported hereafter. Under specific circumstances mechanical transmission may be as efficient as biological transmission, and should be considered at least as an *alter ego*. Based upon the key-variables of the transmission studies, a mathematical model was developed, for a better understanding of mechanical transmission and for further predictive applications [11]. In the present paper we review the experimentation, the mathematical modelling and applications which were done; we discuss the perspectives of further experimental work required to elucidate the exact role of stomoxes in mechanical transmission, and we design a project aiming at gathering the mathematical models of transmission and diffusion of pathogens in a more general model.

We have focussed our study on trypanosomes, but it must be clear that since mechanical transmission is typically a model of "non-specific carrying system", most of the observations would be applicable to any pathogen (including protozoa, bacteria, viruses, and possibly prion proteins) presenting in the blood of a host a substantial amount of circulating infecting particles that can be picked up, transferred, and inoculated to another host by a biting insect. Thus, they can be local vectors of any exotic disease mechanically transmitted.

Materials and methods

Transmission experiments:
Three experiments on mechanical transmission were conducted in Lahirasso (Burkina Faso), nearby a village with a very low density of tsetse flies but with high tabanid pressure. The complete design of these experimentations has been published [8-10]. Ten heifers (crossbred Zebu X *Baoulé*) that were 1-2 years old and free of trypanosome infection were kept together in a 10 m by 10 m square corral. To avoid any feeding by tsetse flies, the corral was entirely covered by a mosquito net (12 m by 12 m), and a screen system was created at the entrance. Two of the heifers (referred as "donor heifers") were experimentally infected with local stocks of *T. vivax* (experiments 1 and 2) or *T. congolense* type savannah (experiment 3). The other heifers were referred as "recipient heifers". In each experiment a single Tabanid species was used: *Atylotus agrestis* (experiments 1 and 3) or *A fuscipes* (experiments 2); the insects were trapped with Nzi traps in the surrounding of the experimental site, identified, counted

and introduced daily into the fly proof corral. Heifers were bled daily for counting of parasites, PCR on buffy coat and serological examinations to follow-up the infection and determine daily incidence.

Modelisation of the parasitaemia

To allow development of a general model, a typical profile of the daily variations of the parasitaemia in a *T. vivax* infection was designed by modelling the observed daily parasitaemia in 20 cattle experimentally or naturally infected. This profile was substituted to the real parasitemic profiles in the mathematical modelling.

Mathematical modelling of transmission

We developed the mathematical model of pathogen transmission by a defined tabanid population, based on (i) the parameters daily available from our experiments: parasitaemia, number of insects, number of cattle, daily prevalence, and (ii) estimated constant which stands for all unknown parameters [11].

Results

Transmission experiments:

In these 3 experiments, transmission of trypanosomes by tabanids was successful, with various incidences, from 25% to 85% within 20 days of exposure of the 10 heifers to daily known numbers of tabanids, ranging from 20-50 insects per head. Parasitaemia of animals was recorded daily from donors and receivers. When applying the following mathematical model, it was observed that the constant C had a similar value in all 3 experiments.

Modelling of the parasitaemia

Based on the average parasitaemia in 20 experimental or natural infections, a typical *T. vivax* daily parasitaemic profile was edited, as shown in **figure 1**.

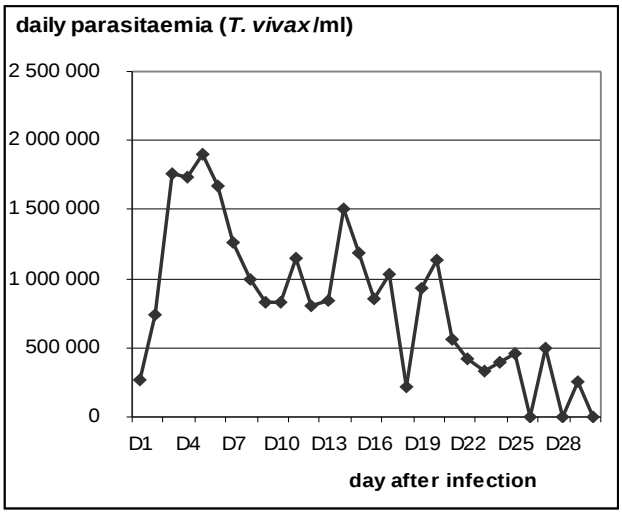

Figure 1: Parasitaemic profile of *T. vivax* infection in cattle

Mathematical modelling of transmission

The aim of the model was to represent the number of new infections expected per day, due to the mechanical transmission of trypanosomes among a group of *N* hosts, under a burden of *n* insects. The prevalence observed after an exposure period of *d* days, $Prev_d$, was:

$$Prev_d = Prev_0 + \sum_i^d n_i \times C \times T_i \times (N - Inf_{(i-1)}) / N^2$$

where *d* is the duration of the exposure (in days), n_i the number of insects at day *i*, T_i the total parasitaemia of the *N* hosts at day *i* (expressed in number of parasites/nl of blood) and $Prev_0$ the initial prevalence. The constant C which gathers unknown parameters of the pathogen system (host/ parasite/ vector), was the mean value out of the 3 experiments.

When the model was run with the parasitaemic profile the evolution of incidence and the final prevalence were similar to that of the experiments themselves, showing that this profile was acceptable for our model.

This predictive model allowed simulating the evolution of prevalence under various circumstances (initial prevalence, insect densities, insecticide or parasitic treatment applied, etc). Figure 2 and 3, show the evolution of the prevalence in herds of 30 cattle under a daily burden of respectively 15 and 60 biting insects. Prevalence at day 40 reached respectively 35% and 100%, showing the determinant role of the insect burden and the very high efficiency of mechanical transmission.

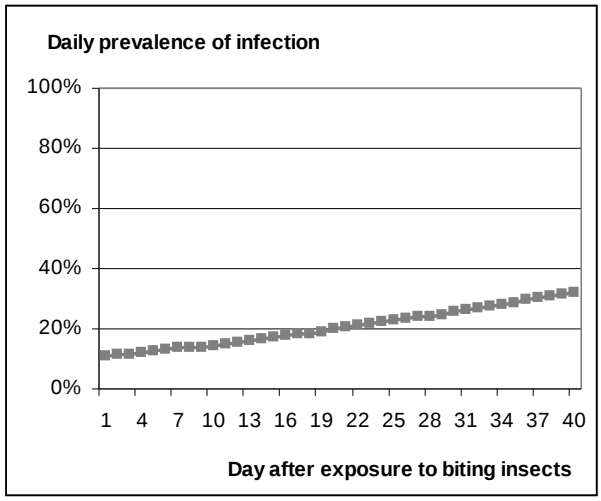

Figure 2: Daily prevalence of *T. vivax* infection in a herd of 30 cattle with initial prevalence of 10%, under a daily burden of 15 biting insects / head.

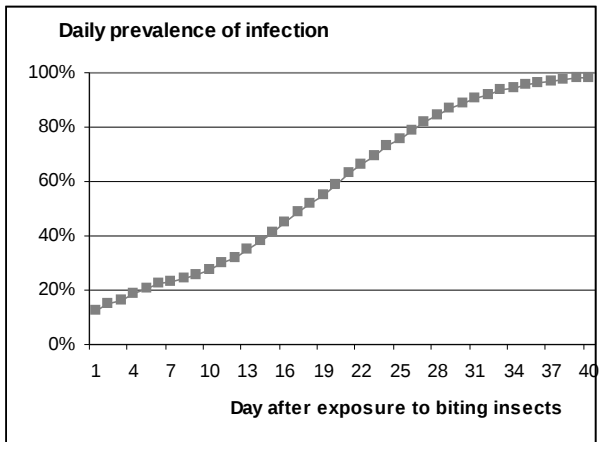

Figure 3: Daily prevalence of *T. vivax* infection in a herd of 30 cattle with initial prevalence of 10%, under a daily burden of 60 biting insects / head.

Discussion and perspectives

This work allowed modeling the disease transmission by tabanids as mechanical vectors, based on the daily pathogenemia, the mean individual insect burden, the herd size and the initial prevalence of infection, using a defined pathogenemia profile. The latter is a model of daily evolution of the pathogenemia in the host which is necessary to establish in order to adapt this model to other pathogens. Infectious dose of the pathogen under study is another required parameter. Based on these data, such models could be developed for other pathogens.

Similar work is being initiated with stomoxes (stable fly). In a series of experiments, the ability of *Trypanosoma evansi*, *Besnoitia besnoiti*, Lumpy Skin Disease virus and Bluetongue virus will be evaluated for mechanical transmission by *Stomoxys* sp. Non-infected and infected lambs or heifers will be put together for 3 weeks in a fly proof corral with a known daily burden of stomoxes. Kinetic of transmission will be observed and modelled based on daily prevalence, pathogenaemia and insect number. Once this work will be done, a more generic model of pathogen transmission by biting insects (tabanids and stomoxes) will be developed.

The ultimate step will be to study the geographical diffusion of mechanically transmitted diseases by animal movements and trading. We will construct a network with farms, grazing fields and markets as nodes, and movements and trading relations linking them, as edges. At the herd level, we will simulate the mechanical transmission using the generic model previously developed. At the geographical level, the diffusion of hosts (migration of animals, trading…) will be simulated using a Discrete EVents System (DEVS) specification [12]. The model will be similar to gravity or percolation models, where the flow between nodes simulates animals movements. In this particular context, a DEVS model better capture the irregular and discontinuous nature of movements at the geographical scale. We will demonstrate the feasibility of the model with a theoretical application developed in specialized platform [13]. If adjustments of parameters are provided, such model could be applied to many pathogens present in the blood of their hosts (Bovine Leukemia virus, *Anaplasma* among others).

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