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Analysis of the population structure of *Plasmodium falciparum*-infected erythrocytes

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Infections caused by *Plasmodium falciparum* comprise highly heterogeneous parasite populations. Asynchronism in the intraerythrocytic cycle is one of the causes of cellular diversity among the infected erythrocyte forms.

The distribution of infection stages among *Plasmodium falciparum*-infected red blood cells is an apparent measure of the population structure. This can be used for characterizing the state of the infection process and for better predicting its dynamics. It is also an essential tool for comparing different infected blood samples. This can be used for testing the efficiency of treatments in drug trials and for better understanding host-pathogen interactions, among others.

Population diversity can be quantitatively assessed by using theoretical tools such as the Shannon diversity index, and it can be reproduced by Individual-based models (IbMs) of the population, which constitute a consistent method for understanding how cellular mechanisms give rise to the observed macroscopic patterns. A simple scenario to study how population structure affects infection dynamics is the continuous static *in vitro* cultivation of the parasite.

The joint application of statistical thermodynamics, mathematical modelling and experiments allowed for the distinction of temporal scales characteristic of the infection on the whole of the order of 10 days. This is five times the temporal scales characteristic of the infection cycle (~48 hours). The analysis of the mechanisms leading to the diversity observed in real systems provides with a more complete understanding of the infection on the whole (see Figure).

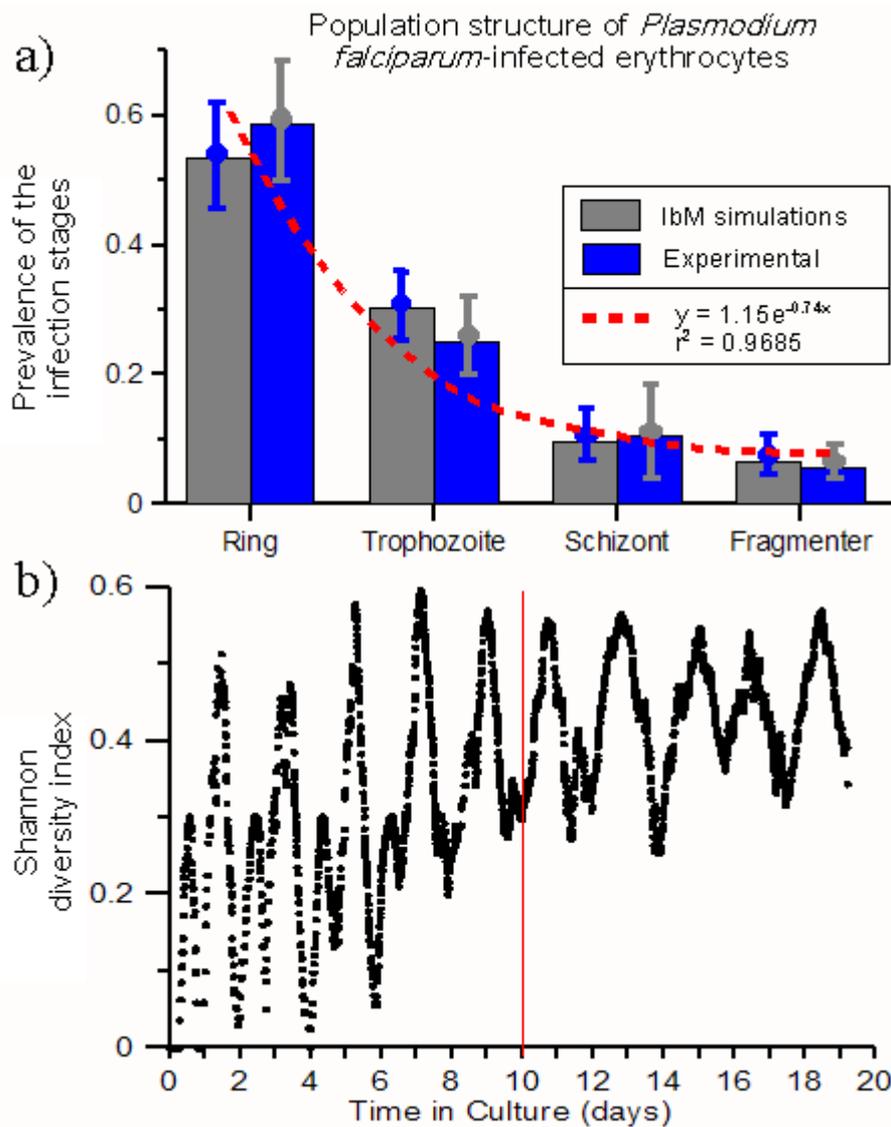


Figure: (a) Prevalence of the infection stages over a complete cultivation lasting 20 days with periodic subcultivations. IbM simulation outcomes are compared to the experimental results from Trager and Jensen (1976), and fitted to an exponential decay. (b) Simulated evolution of the diversity of infected forms. The vertical solid line indicates the temporal scale characteristic of the relaxation of the population structure.

Keywords: *Plasmodium falciparum*, Population structure, Shannon diversity, Individual-based model