

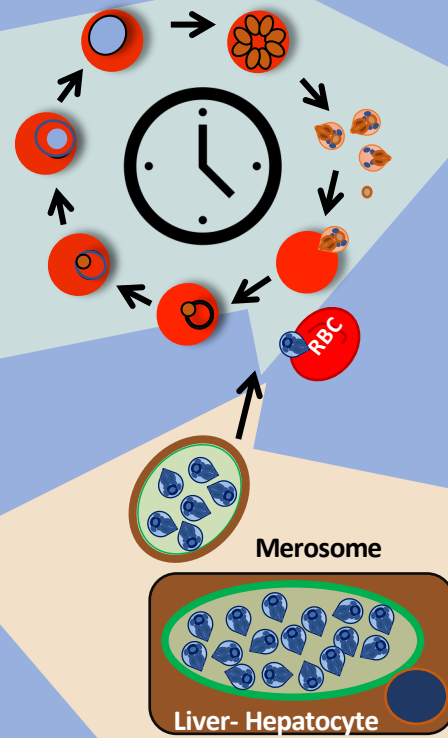
Chronicles of Plasmodium: the parasites' journey through the liver and into the blood

Alejandra Herbert-Mainero*, Aidan J. O'Donnell, Petra Schneider, Sarah E. Reece
 Institute of Evolutionary Biology, School of Biological Sciences, University of Edinburgh, UK. *a.herbert-mainero@sms.ed.ac.uk

Plasmodium parasites have a complex life cycle that involves replication in multiple sites in the host

BLOOD

Asexual replication within red blood cells is rhythmic in most *Plasmodium* species. Transitions between intraerythrocytic developmental (IDC) stages are synchronized to host feeding-fasting rhythms^{1,2}. The liver is responsible for most metabolism-related rhythms³, **yet it is unknown whether feeding-fasting rhythms matter to liver-stage parasites.**

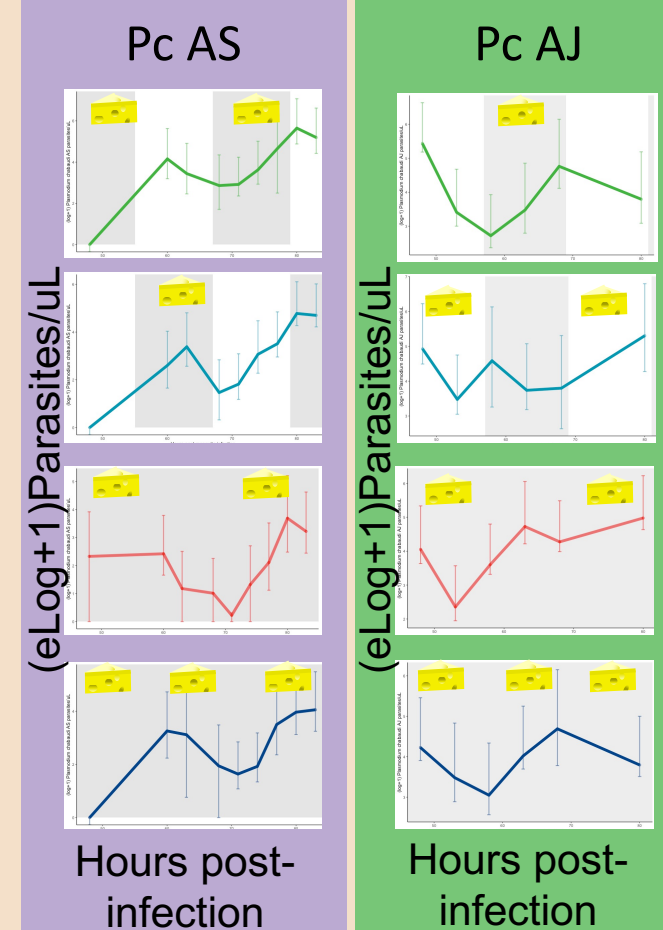
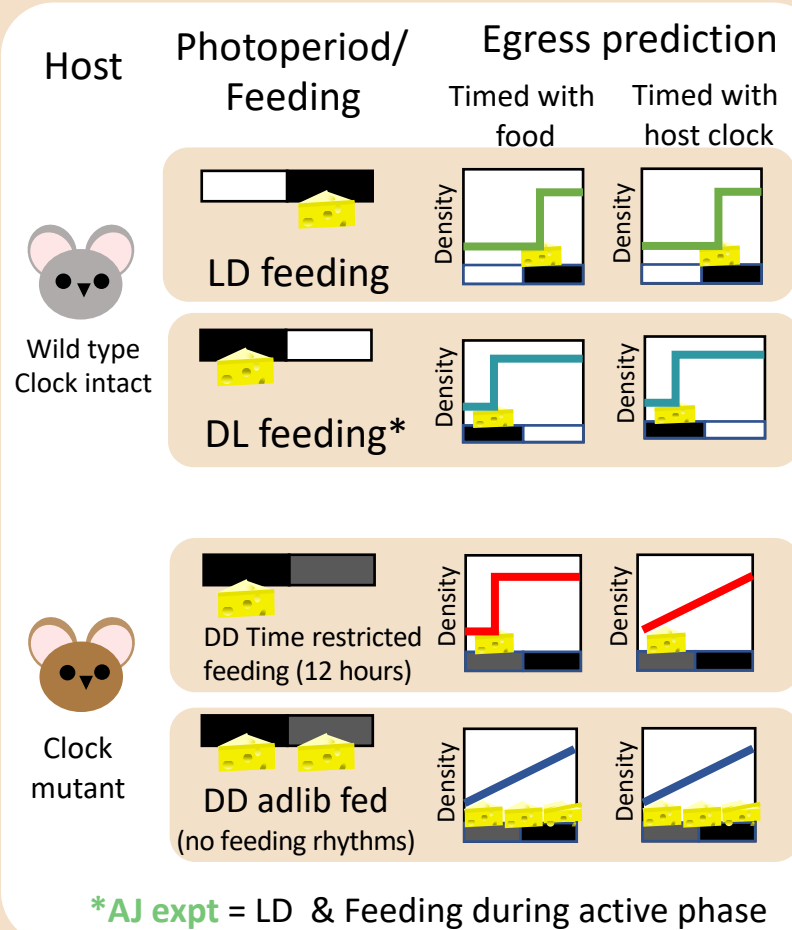
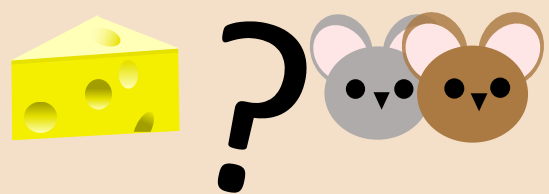


LIVER

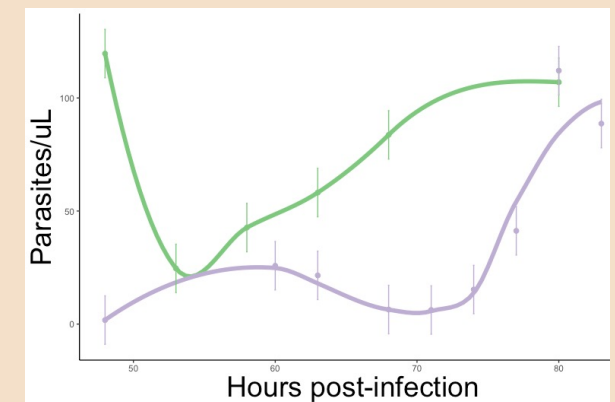
We use *P. chabaudi* to test whether:

- Liver-stage parasites exploit metabolic rhythms for their development / egress
- Synchronizing egress with host rhythms allows blood stage replication to begin "on time"
- Natural egress patterns are beneficial for the parasite or an evolutionary constraint

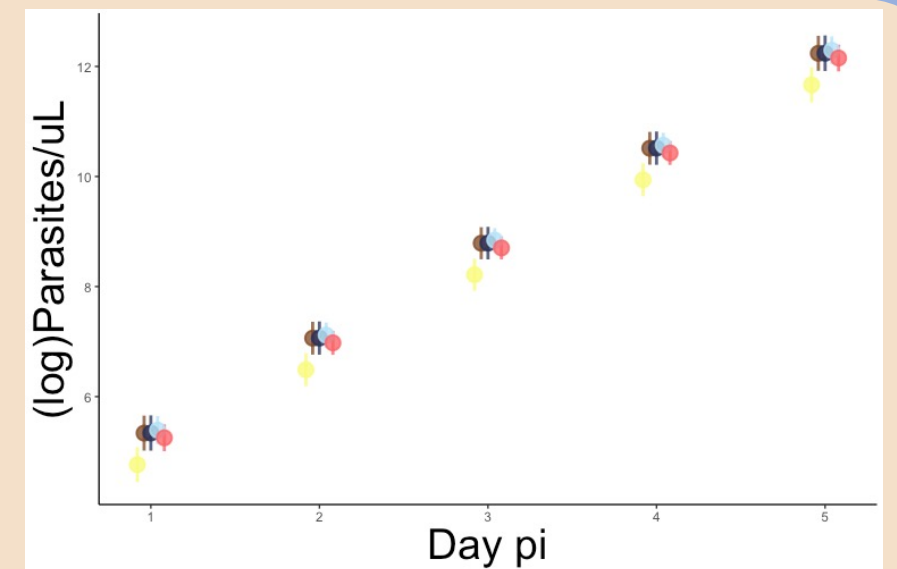
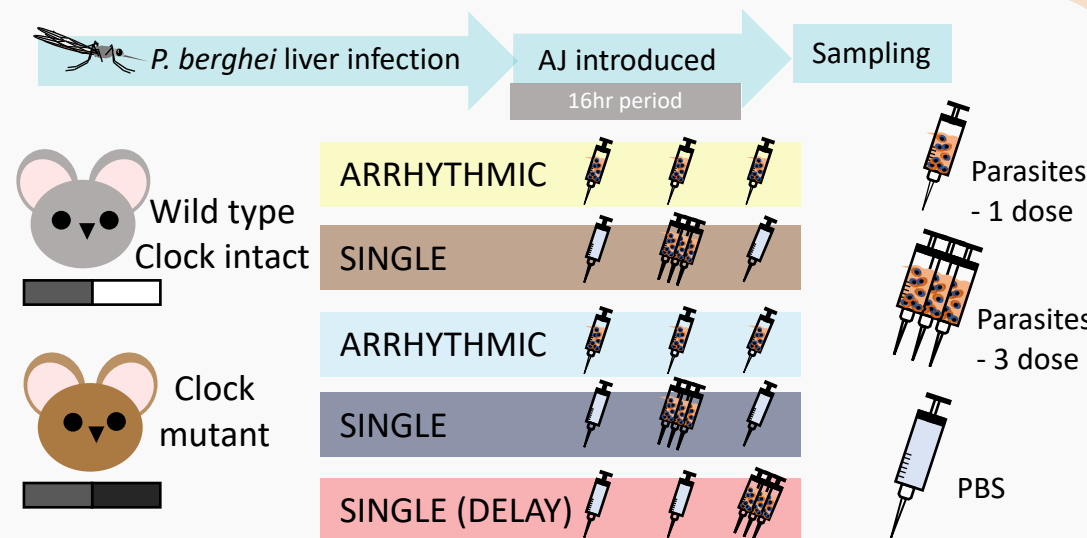
Is egress of *P. chabaudi* **AS** and **AJ** (indirectly measured as the accumulation of parasites in the blood) determined by duration or related to host feeding/fasting rhythms or host clocks?



Egress is independent of all host rhythms (**AS**, $F_{3,179.08}=1.23$ and **AJ**, $F_{3,445.95}=1.03$) and follows a non-linear pattern set by developmental duration. **AS** egresses later and slower.



Do blood stage infections perform better if introduced into the blood on multiple occasions over 24 hours (arrhythmic) or in a single burst?



CONCLUSIONS

- Blood stage accumulation is arrhythmic and independent of host clock- and feeding-rhythms
- Establishment in the blood is not affected by egress pattern
- Parasites organize IDC schedule during first cycles of blood stage replication⁴

WHY CARE ABOUT LIVER EGRESS PATTERNS?

- Rhythmicity is a specific adaptation to the blood-stage of infection
- Timing mechanism for the IDC is not used in the liver stage
- Time of day of transmission is changing (due to bed nets) but this may not impact on disease severity due to a fixed developmental duration for the liver phase and no relevance of egress timing.