Mechanosensory pathways as a potential target for vector control in malaria

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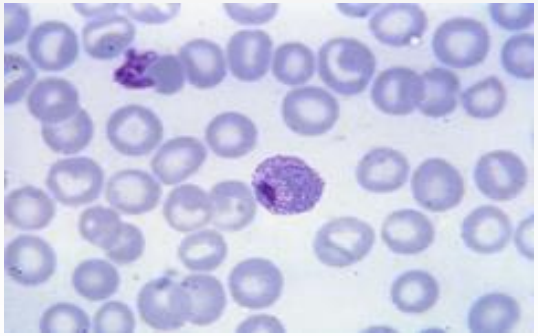
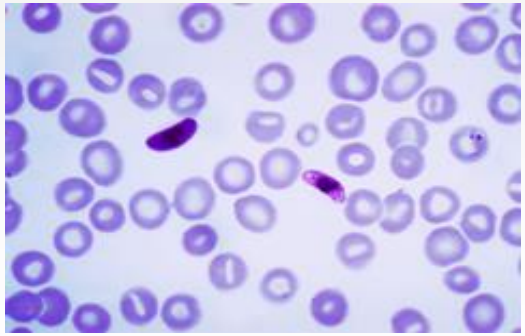
Malaria

- Caused by *Plasmodium* protists
- *P. vivax* and *falciparum* are the most significant for humans
- Spread by mosquitoes of the family *Anopheles*



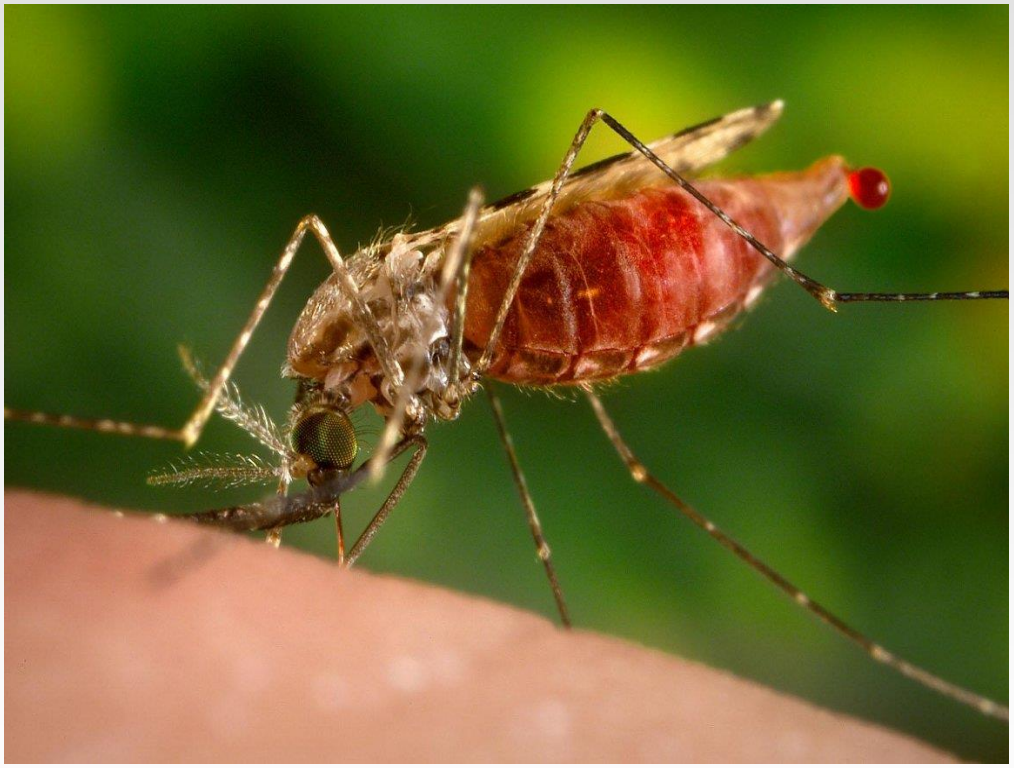
Plasmodium vivax



Plasmodium falciparum

Mosquito vector

- Different *Anopheles* species act as vector in different locations
- Studies often use *A. stephensi* because easiest to raise



Anopheles female feeding

Significance of malaria

- Symptoms include fever, convulsions and kidney failure – severe cases can lead to death
- Estimated 219 million documented cases of malaria in 2010 according to WHO
- Approximately 650,000 mortalities, the majority of which were children
- Increased range of vector due to climate change

Current methods for eradication

3 different methods to combat malaria:

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Protect humans from infection using vaccines

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Treat infected with antibiotics

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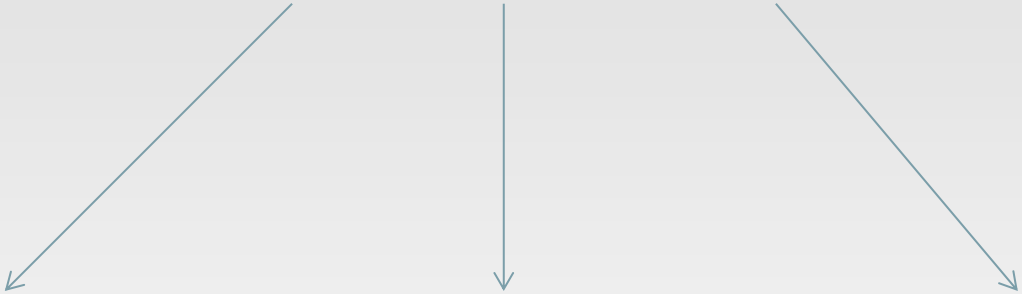

Protect humans from infection using vaccines

Treat infected with antibiotics

Target vectors with insecticides

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3 different methods to combat malaria:

Protect humans from infection using vaccines

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Target vectors with insecticides

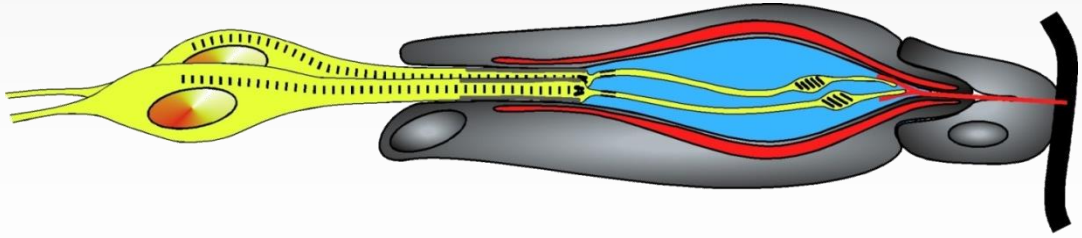
Many insecticides that lead to loss of mechanosensation are available but untested for application against malaria vectors

Mosquito chordotonal organs

- Male Johnston's organ is largest chordotonal organ in all insects – has over 7000 scolopidia

- Female has significantly smaller organ (approximately 3000 scolopidia)

Scolopidia



Importance of mechanosensation

- Insertion of the proboscis whilst blood feeding is very likely to require some sort of mechanosensory feedback
- Courtship takes place whilst mosquitoes are flying and involves acoustic communication
- Therefore insecticides which are able to target mechanosensation could be useful

Pymetrozine

- Significant efficacy against aphids and other insects at concentrations as low as 1 part per ten million
- Leads to loss of all chordotonal organ function
- Mechanism of action is unknown
- Aphids cannot insert proboscis into plants after exposure to pymetrozine

Pea aphid feeding on plant

Female *A. stephensi* during blood meal

Project aims

Study the mechanosensory basis of, and requirements for,

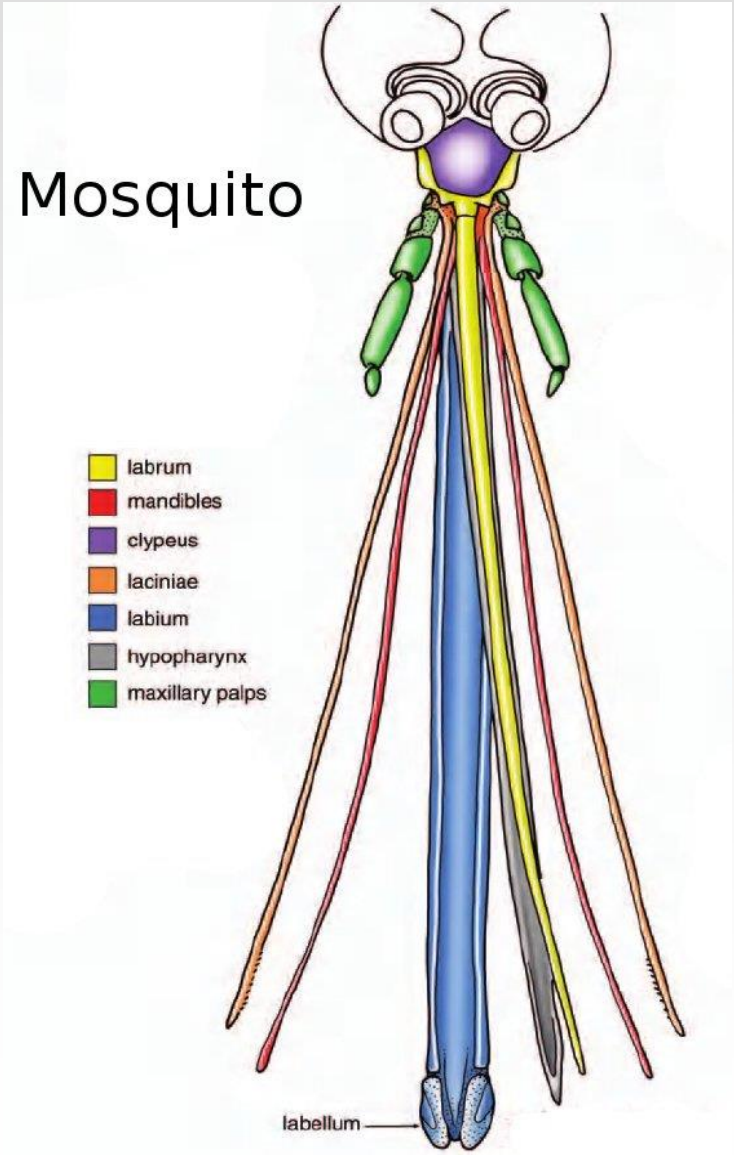
i) blood-feeding

ii) mating

in mosquitoes and the effect on these important parts of the mosquitoes life cycle of insecticides that destroy chordotonal organ function

Current and proposed experiments

- Investigate using water as a solvent for pymetrozine
- Take high speed camera footage of biting by mosquitoes injected with pymetrozine
- Investigate the impact, if any, of pymetrozine on the ability to mate



- Dissect mosquito mouth parts to investigate chordotonal organ distribution

Proposed mathematical modelling

Goal = Create a model that accounts for the effect of mechanosensory impairment on the mosquito to investigate the potential impact of using pymetrozine

Tools = No completely suitable malaria models exist currently

A model by Lynch et al. (2012) including fungal insecticide could be adapted for this purpose

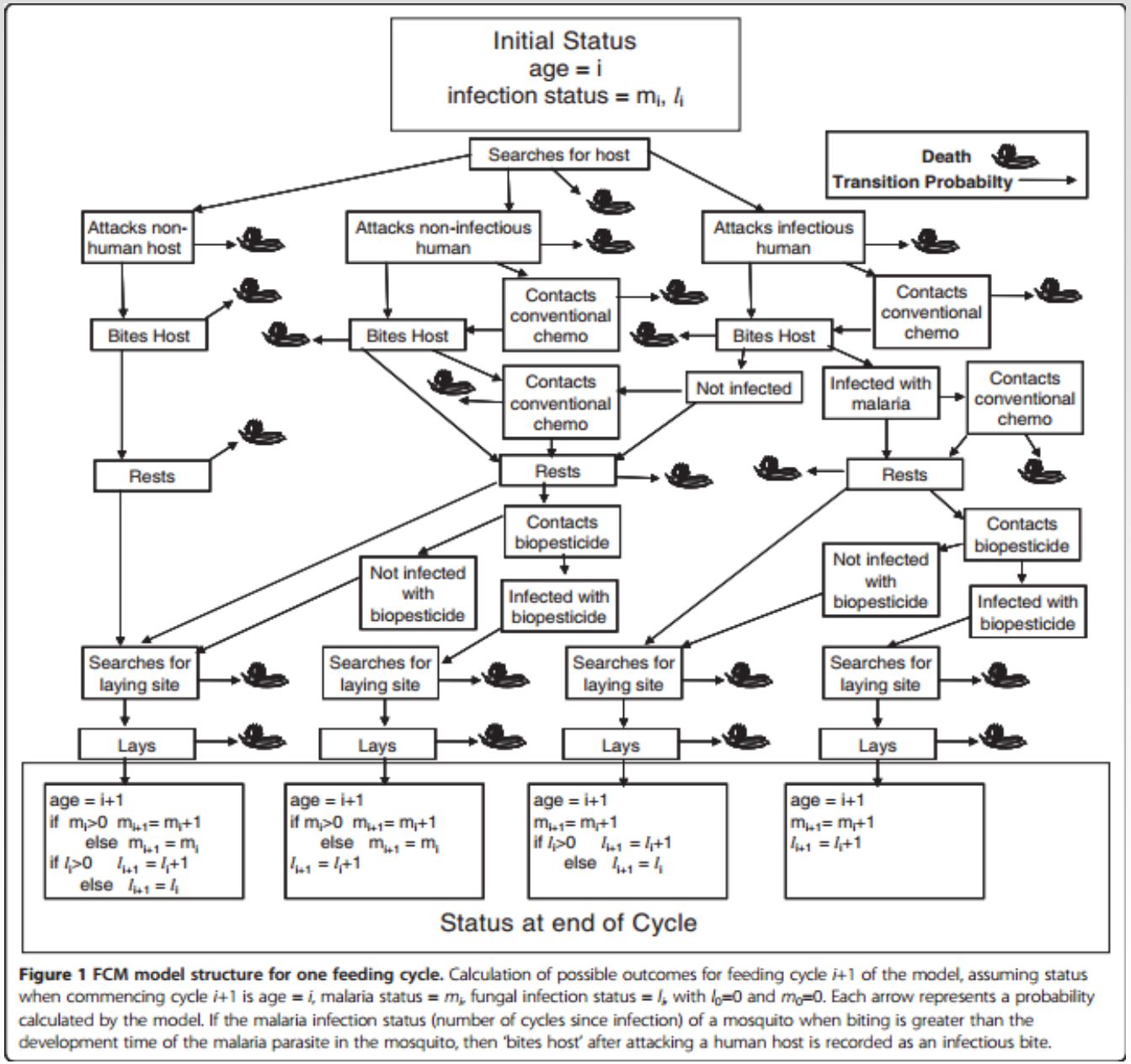


Figure 1 FCM model structure for one feeding cycle. Calculation of possible outcomes for feeding cycle i+1 of the model, assuming status when commencing cycle i+1 is age = i, malaria status = m_i, fungal infection status = l_i, with l_0=0 and m_0=0. Each arrow represents a probability calculated by the model. If the malaria infection status (number of cycles since infection) of a mosquito when biting is greater than the development time of the malaria parasite in the mosquito, then 'bites host' after attacking a human host is recorded as an infectious bite.

Conclusions

- New insecticides are needed to combat malaria
- Insecticides that affect mechanosensation have a number of promising advantages
- Greater understanding of the role of mechanosensation for blood feeding and mating could be useful in many different respects

Acknowledgements

- Joerg Albert (who helped source all images used)
- Maria-Gloria Basáñez
- Martin Walker

British Heart Foundation

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