

Supplementary Material: Model-based Inference From Multiple Dose, Time Course Data Reveals *Wolbachia* Effects on Infection Profiles of Type 1 Dengue virus in *Aedes aegypti*.

Caetano Souto-Maior¹^{*}, Gabriel Sylvestre²^{*}, Fernando Braga Stehling Dias³, M. Gabriela M. Gomes^{4,5} Rafael Maciel-de-Freitas²


1 Instituto Gulbenkian de Ciência, Oeiras, Portugal


2 Laboratório de Mosquitos Transmissores de Hematozoários, Instituto Oswaldo Cruz, Fiocruz, Rio de Janeiro, Brazil

3 Gabinete da Presidência, Fiocruz, Rio de Janeiro, Brazil

4 CIBIO-InBlo, Centro de Investigação em Biodiversidade e Recursos Genéticos, Universidade do Porto, Porto, Portugal

5 Liverpool School of Tropical Medicine, Liverpool, United Kingdom.

 These authors contributed equally to this work.

 current address: National Heart, Lung, and Blood Institute, Bethesda, MD, USA

* correspondence: caetanosoutomaior@protonmail.com

Mosquito numbers and subgrouping data tables

A total of 616 mosquitoes were divided by symbiont status (absent, *wMelTET* colony, and present *wMelBR*) into two groups of approximately half that size, and challenged with five different *DENV-1* doses plus mock-infected controls injected with culture medium. These numbers are shown in table A.

Table A. Number of mosquitoes challenged and assayed for viral titers

	time point	dose (TCID ₅₀ /ml)					ctrl	total
		10 ⁴	10 ⁵	10 ⁶	10 ⁷	10 ⁸		
<i>wMelTET</i> challenged	all	54	51	55	49	57	38	304
<i>wMelTET</i> qPCR assayed	3 d.p.i.	9	3	8	12	8	8	48
	7 d.p.i.	12	3	8	10	9	1	43
	14 d.p.i.	4	3	7	6	14	3	37
	all (row sum)	25	9	23	28	31	12	128
<i>wMelBR</i> challenged	all	51	57	55	54	55	40	312
<i>wMelBR</i> qPCR assayed	3 d.p.i.	12	11	9	9	13	11	65
	7 d.p.i.	6	10	10	10	10	6	52
	14 d.p.i.	7	4	8	10	14	6	49
	all (row sum)	25	25	27	29	37	23	166

Linear regression for factor effects

We use a generalized linear model as a baseline for significance of the factors included in the experimental design: dose, time, and presence or absence of the *Wolbachia* symbiont. The model is of the following form:

$$\log\mu = \text{dose} + \text{time} + \text{symbiont} \quad (1)$$

errors are assumed to follow a Poisson distribution, like the main model, and significances of the factors were computed with a likelihood ratio test between the model shown above, and a model that does not include any of the terms for which the significance is being tested (e.g. $\log\mu = \text{dose} + \text{time}$ is used as a reduced model to test significance of symbiont presence). All factors showed high significance ($p < 0.001$) under this linear model.

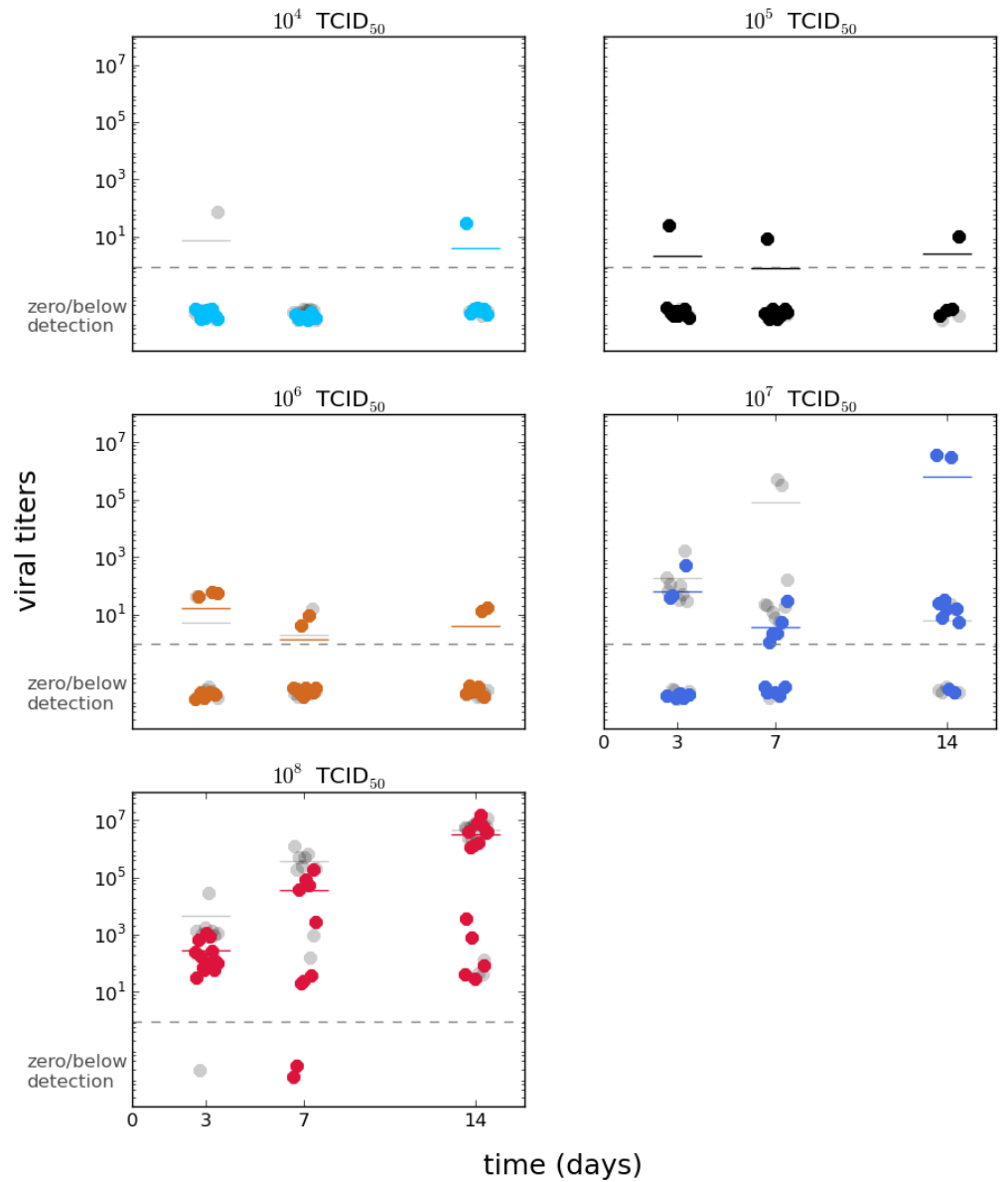


Fig A. Viral levels in symbiont-carrying mosquitoes. DENV-1 viral titer data for *wMelBR* group (colors) overlaid to that of the *wMelTET* group (light gray)

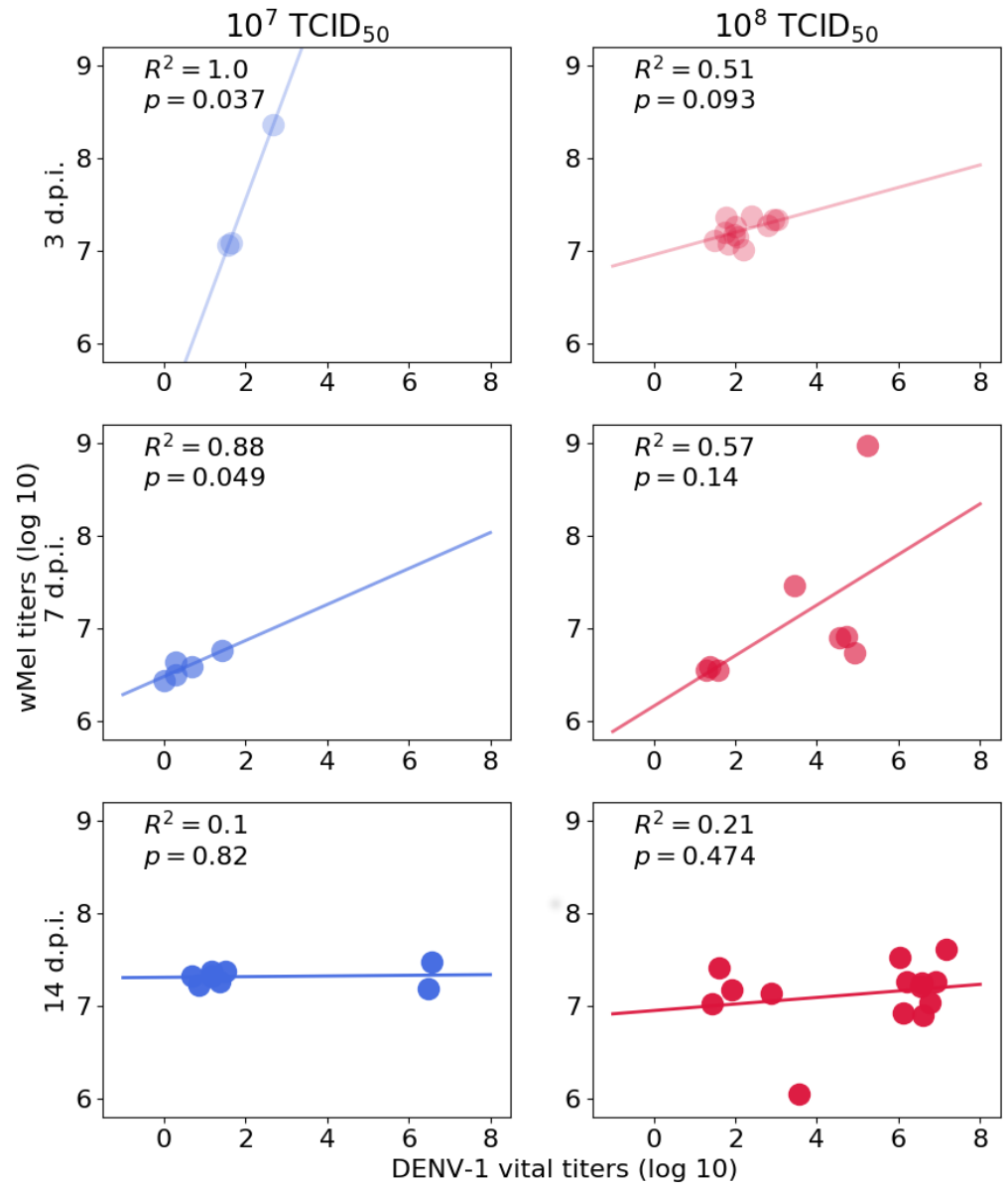


Fig B. *Wolbachia*/DENV-1 level correlation. Correlations between DENV-1 and *Wolbachia* titers displayed as per-dose subsets in separate panels for each dose and time point – color code follows that of the raw data.