Title: Delayed and time-cumulative toxicity of imidacloprid in bees, ants and termites

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Supplementary Information (SI)

The toxicity model can be applied to acute poisoning events as well as the chronic case described in the main text. In the acute case, (Figure S1) the initial dose rapidly binds to receptors as the circulating toxin is metabolized. In Fig S1, a relatively constant level of bound toxin (about 10% of the initial dose) persists and biological damage grows linearly with time because of the hypothesized excitotoxic effects. Doubling the initial toxic exposure will halve the time for the relative biological damage to reach unity (LT50).

The dissociation time of the toxin from the nAChR is not known accurately, only that the toxin binding is strong, implying a relatively long $\boldsymbol{\tau_D}$. If there is slow reversibility of the compound binding to active sites, the level of bound toxin for chronic exposure will sag in time and eventually plateau. Experimentally, this will give rise to a time exponent of two for short durations, transitioning to one for time much longer than $\boldsymbol{\tau_D}$when results are plotted on a log-log graph.

Model results for a variety of $\boldsymbol{\tau_D}$ are plotted along with the honeybee experimental data in Figure S2. For dissociation time much less than 10 days, it would difficult to reconcile the Dechaume-Moncharmont et al. [16] data points with the reported LD50 averages.

Our model would predict that single-dose poisoning experiments will show linear time-dependence similar to Haber's rule, while chronic, continuous-exposure experiments will be closer to t^2 dependence. One factor of time naturally comes from the accumulation of the chronic dose consumed. The best power fit exponents for the two types of experiments, derived from the fitting lines in Figure 2 for the chronic data, and a similar plot (not shown) for LD50 measurements where the selected researchers provided at least three time points, are shown in Table S1. Indeed, the single-dose experiments yield a time exponent close to one.

Figure legends

Figure S1: Toxicity model for an acute 10 ng/bee poisoning event. Ingested toxin is quickly metabolized and eliminated while bound toxin builds quickly to a plateau where the amount of bound toxin is approximately τ_M/τ_D times the initial dose. Biological damage increases approximately linearly with time, rendering a time exponent of 1 (i.e. Haber's rule).

Figure S2: Comparison of the toxicity model for various $\boldsymbol{\tau_D}$ and honeybee experimental data.

Table S1: Imidacloprid time exponents for single dose and chronic studies on bees and ants [12].

Time Exponent	Fit r^2	Type test	Data source
0.84	0.99	Single Dose	24, 48, 72 hr. LD50 [23]
0.79	0.82	Single Dose	48, 72, 96 hr. LD50 [15]
0.93	0.64	Single Dose	averages of several researchers – 24, 48, 72, 96 hr. LD50 [20]
1.73	0.97	Chronic	[12]
1.6	0.98	Chronic	[19]

Figure S1: Toxicity model for an acute 10 ng/bee poisoning event

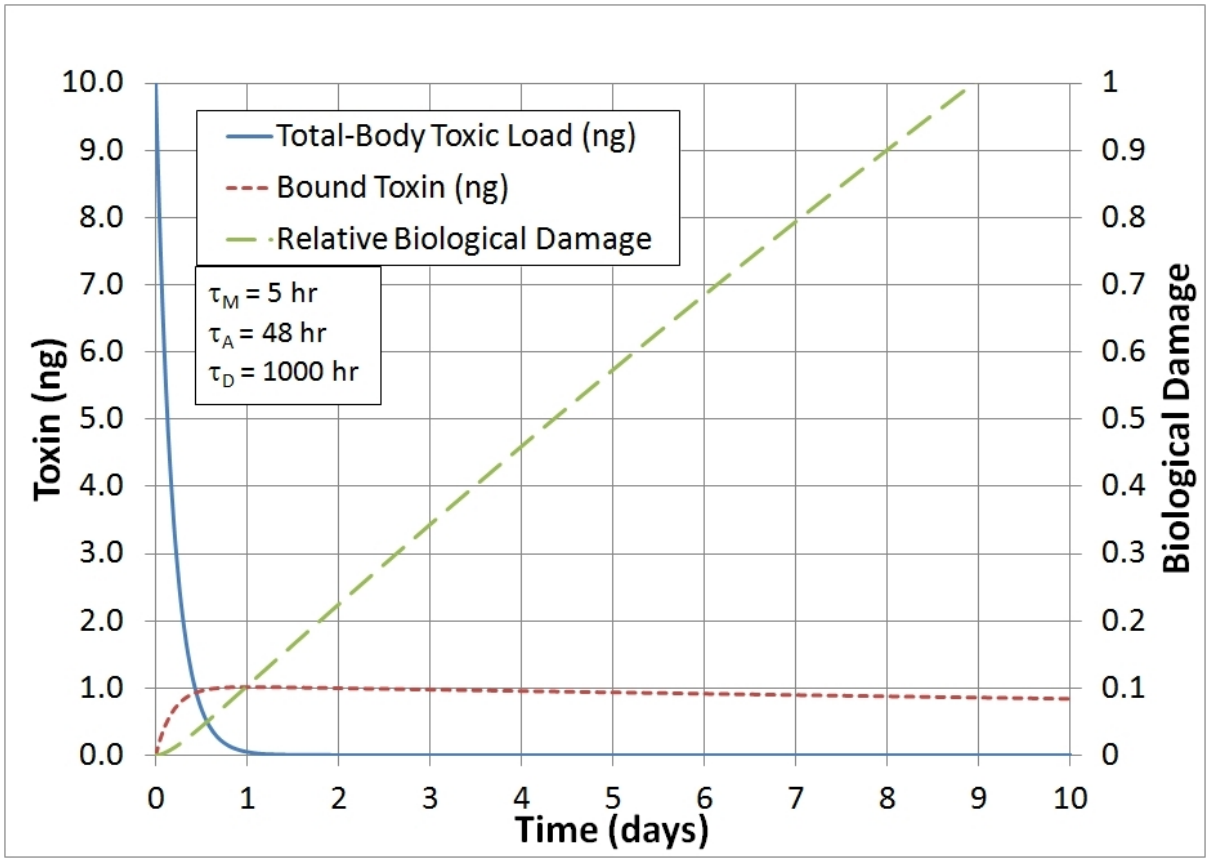

Figure S2: Comparison of the toxicity model for various τ_D and honeybee experimental data.