PhD position available at INRA, Rennes

Mechanistic modelling of reprotoxic effects of pesticides in populations of the freshwater gastropod *Lymnaea stagnalis*

Current concern in environmental risk assessment of pesticides refers to the protection of populations. However, a number of issues need to be solved in order to reach this protection goal. In particular, realistic assessment of population effects in non-target organisms is still difficult to achieve, mainly due to the complexity of exposure and effect / recovery patterns in individuals that are exposed to these compounds. In order to obtain realistic risk forecasts at the population level, we thus need to develop test methods and data analysis tools that are relevant to assess realistic patterns of exposure and biological responses in individuals.

Mechanistic models based on the analysis of toxicokinetics and toxicodynamics (TK-TD) have been identified as promising tools to do so. Yet, most TK-TD models that have been developed to date focus on the modelling of effects on survival, which is not enough to upscale from individual to population level effects. Developing innovative models for the analysis of sublethal responses to toxicants thus constitutes a major challenge.

To date, TK-TD models based on the Dynamic Energy Budget theory appear to be relevant when analyzing and predicting sublethal effects of toxicants in exposed individuals because (i) the DEB theory provides a unified conceptual framework where both effects on the various life-cycle traits of organisms and trade-off between these traits can be accounted for and (ii) model output can directly be used as input data for both refined risk assessment procedures at the individual level and for population effect models.

Yet, some issues that are specific to ecotoxicology remains to be tackle in the DEB framework. For instance, the possibility to model sublethal effects of time-varying concentrations of pesticides with DEB based approach should be studied. Furthermore, the applicability of this approach to describe and predict sublethal responses to low doses of toxicants, which often generate complex response pattern such as hormesis or U-shaped curves, remains to be investigated. At last, one should investigate how this theory can be used to explain complex patterns of individual recovery after exposure ceases.

In this context, this PhD project aims at exploring how the DEB theory could be used as a basis to improve existing TK-TD models for the analysis of biological responses to toxicants, focusing on three key issues for refined risk assessment practices (i) how to deal with complex exposure profiles, (ii) how to deal with subtle and complex responses to toxicants that are active at low doses and (iii) how to account for recovery. Due to the relevance of maturation and reproductive processes for population dynamics, we will focus on responses of juveniles and adults to toxicants. Expected outputs are validated and documented reproduction effect models for individuals, which can be used to predict effects of pesticides on populations.

This PhD project will be based on the coupling of experimental and modelling approaches in the great pond snail (*Lymnaea stagnalis*). This model species is of particular interest since it has been identified by e.g., OECD, as a relevant candidate species for the development of standardized test procedures for the assessment of sublethal effects of chemicals. Results of this doctoral work could thus contribute to consolidate the basis of forthcoming toxicity test guidelines with this snail.

Sublethal responses to pesticide exposure will be quantified through partial life-cycle tests in the laboratory regarding snail growth, development and reproduction. We will focus on the study of reproductive responses to low doses of toxicants, which are of particular concern in risk assessment. Partial life-cycle toxicity tests will be specifically designed in order to allow answering the three main PhD issues that were identified above. In these studies, the amount and quality of food will be taken into account, since the interaction of food and toxicants might influence the dose-response relations. Toxicity test results (*i.e.* exposure, effect and recovery patterns) will be interpreted within the framework of the DEB theory. This may require adapting the physiological assumptions underlying the currently available models. Finally, the impact of sublethal effects, as modelled at the individual level, will be extrapolated to the population level (departing from existing modelling approaches).

Corresponding PhD objectives are:

- To identify, based on previous work carried out at the INRA and a sound literature analysis, chemicals that generate reprotoxicity at low doses in non-target aquatic molluscs;
- To investigate response patterns (effects and recovery) of the pond snail to selected chemicals using partial life-cycle experiments in the laboratory;
- To gain experience with current DEB models on toxicity data, and to modify these models, when necessary, in order to ensure that they can adequately explain reprotoxic effects of pesticides and recovery patterns in the pond snail;
- To use existing modelling approaches to upscale from individual to population-level effects of toxicants
- To implement and describe the models in agreement with good modelling practices and produce the corresponding TRACE documentation.

This "DEB-2" PhD project will be closely connected to the "DEB-1" PhD project, supervised by T. Jager at the Vrije Universiteit Amsterdam (Netherlands). The DEB-1 PhD project focuses on investigating, in a DEB framework, how the effects of toxicants on the embryonic development of *L. stagnalis* may lead to changes in the population dynamics. Overall, findings form the DEB-1 and DEB-2 projects will contribute to provide a generic modelling framework that could be ultimately applied to other species to evaluate population effects of chemicals.

Candidates should be interested in aquatic ecotoxicology and mathematics, and in the coupling of laboratory experiments and modelling approaches. Basic skills in ecological modelling are desired, and will be complemented by attendance of advanced training courses / workshops in ecological modelling proposed by the CREAM initial training network, as well as working visits to the co-supervisor (T. Jager). Basic ecotoxicological knowledge is also desirable, and will be complemented by appropriate training courses during the PhD.

The experimental part of the work will be implemented in the Ecotoxicology and Quality of Aquatic Environments research group (INRA, Rennes - www.inra.fr), under the supervision of V. Ducrot (virginie.ducrot@rennes.inra.fr). Experimental facilities and technical staff will be provided to support the PhD activities at the INRA. The modelling work will be performed in close collaboration with the Theoretical Biology Department of the VU Amsterdam, under the supervision of T. Jager (tjalling.jager@falw.vu.nl). Therefore, the motivation and ability to cooperate in a research consortium is required.

The PhD thesis will be defended both in France and in The Netherlands, enabling the candidate to obtain a Double Doctorate graduation. Furthermore, the candidate will benefit of all activities included in the CREAM network, leading to an advanced level initial training, which will facilitate obtaining a position in academia and governmental institutions or industry after graduation.

The position is available on October 2010
Duration: 3 years
Salary and terms of employment will be in accordance with Marie Curie rules of the European Commission (http://ec.europa.eu/research/mariecurieactions/careers_en.htm)
Please note that French candidates are not eligible

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