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Hill coefficient-based stochastic switch-like signal directly governs damage-recovery dynamics in freshwater fish in response to pulse copper

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ABSTRACT

Growing evidence demonstrates that fluctuating metal stressors can have profound impact on the ecophysiological responses in aquatic species. However, how environmental stochasticity affects the complex damage-recovery dynamics in organisms remains difficult to predict. The objective of this paper was to investigate the stochastic behavior in the damage-recovery dynamics in tilapia in response to pulse waterborne copper (Cu). We developed a mathematical framework that allows discrimination between damage and recovery processes in tilapia exposed to designed pulse Cu scenarios. We built deterministic nonlinear models for the damage-recovery dynamics that produce response surfaces describing killing/recovery rate–Cu-pulse interval interactions. Here we showed that the stochastic switching behavior arose from competition among killing, recovery rates, and Cu pulse frequency. This competition resulted in an ultrasensitivity appeared in whole body, gills, muscle, liver, and kidney with Hill coefficients of ≥7, 4, 7, 5, and 5, respectively, at Cu 3 mg L^{-1}, dilution rate 0.05 h^{-1}, and pulse interval 72 h, indicating that a stochastic switch-like response was generated. We argue that the role of gill-associated Hill coefficient as a direct signal of the stochastic switch-like response in the damage-recovery dynamics in response to pulse metal stressor can serve as a sensitive indicator for risk detection in fluctuating environments. Our approach constitutes a general method to identify the stochastic switch-like response for aquatic species exposed to fluctuating metal stressors, which may help to predict and, eventually, expand our understanding of the damage-recovery dynamics. Finally, we implicate that Hill coefficient-based switch-like signal and its damage with hazard response can be linked in an information theoretic framework to handle environmental stochasticity.

1. Introduction

The association between aquatic species exposed to fluctuating or pulsed contaminants and their responses has been extensively studied in a wide variety of systems, demonstrating that fluctuating metal stressors can have profound impact on the ecophysiological responses (Meyer et al., 1995; Reinert et al., 2002; Diamond et al., 2006; Ashauer et al., 2007, 2010; Chen and Liao, 2012; Chen et al., 2012a,b). Recently developed model used to describe the survival process of aquatic species in response to fluctuating and sequential pulses of contaminants is a process-based threshold damage model (TDM) based on the damage assessment model (DAM) (Ashauer et al., 2007, 2010). They argued that the sequence where organisms are exposed to chemicals could matter as important as the concentration and exposure duration.

Chen et al. (2012b) have incorporated a positive damage feedback loop into a toxicokinetic/toxicodynamic (TK/TD)-based TDM to assess susceptibility for tilapia and freshwater clam in response to waterborne arsenic. They indicated that TDM with positive feedback frequently exhibited a switch-like behavior when exposure levels of metal stressor exceed certain thresholds. On the other hand, different metal stressors with specific Hill coefficients evoke different dynamic patterns of damage with hazard. Moreover, Hill coefficient that derived from a mortality-time profile is suggested as a risk indicator for assessing the survival probability for aquatic species exposed to waterborne metals.

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Chen et al. (2012b) further indicated that the positive damage feedback mechanism could be triggered at or above a Hill coefficient threshold of 4 for tilapia and freshwater clam in response to waterborne arsenic. The Hill coefficient derived from a Hill function-type dose–response profile is larger than 1 is referred to as ultrasensitivity (Koshland et al., 1982; Kim and Gelenbe, 2012).

The ultrasensitivity can be employed to the activating–deactivating damage systems. This general applicability across a range of metal concentrations for the damage response system and the interconvertibility between metal toxicity-induced damage and recovery time make the switch-like behavior an additional factor in ecological risk assessment strategy. An unresolved central question, however, is whether the observed switch-like behavior originates mainly from environmental stochasticity (Chen et al., 2015), or whether it stems from a deterministic process in the DAM that only appears to be random.

In this paper, we used freshwater tilapia *Oreochromis mossambicus*, an important food fish for the people of Taiwan, as the studied fish species. It is also one of the most abundantly invasive species in local freshwater and estuary ecosystems. Typically, tilapia growers in Taiwan used copper sulfate ($CuSO_4$) to exterminate phytoplankton for controlling skin lesions and gill disease (Carbonell and Tarazona, 1993; Chen and Lin, 2001; Chen et al., 2006). Consequently, Cu burdens in tilapia are relatively higher, ranging from 1.524 to 18 $\mu g\, g^{-1}$ dry wt (Lin et al., 2005).

The treatment of culture ponds with >1 $mg\, L^{-1}$ $CuSO_4$ is effective in killing algae and parasites (Banerjee et al., 1990; Boyd, 2005; Mischke and Wise, 2009; Miao et al., 2011). Grosell and Wood (2002) and De Boeck et al. (2007) indicated that high Cu burdens were likely to pose mortality risk for fish due to disruption of branchial ion regulation. Chen et al. (2012a,b) further revealed that pulse frequency or duration were more likely to alter survival probability and population growth in tilapia in response to waterborne Cu.

Our goal was to investigate the stochastic switch-like behavior in the damage-recovery dynamics in tilapia in response to pulsed waterborne Cu. In this paper, we developed a mathematical framework that allows discrimination between damage and recovery processes in tilapia in response to the designed pulsed waterborne Cu settings. A TK/TD-based TDM with a Hill function-based positive damage feedback model was used to examine the complex mechanisms of pulse Cu susceptibility in tilapia. Finally, we built deterministic nonlinear models for the damage-recovery dynamics that produce response surfaces describing killing/recovery rate–Cu-pulse interval interactions.

Understanding this contribution to a dynamic response on a systems scale is essential both for depicting how aquatic species deploy regulatory processes to accomplish ecophysiological changes and for examining key damage-recovery dynamics controlling each process in response to fluctuating metal stressors.

2. Materials and methods

2.1. Study data

The TK data obtained from the sequential pulse Cu exposure experiments (Chen et al., 2015) and mortality data obtained from the Cu acute toxicity bioassays on tilapia population (Nussey et al., 1996) give us an opportunity for examining the switch-like response in the damage-recovery dynamics in tilapia to pulse Cu.

Briefly, Chen et al. (2015) conducted 10-d sequential pulse Cu exposure bioassay to determine pulse Cu accumulation, by using adult tilapia *O. mossambicus* to Cu concentrations by increasing from 100 to 300 $\mu g\, L^{-1}$. The pulse Cu exposure timings were occurred twice during the exposure periods at hours 24 and 144, respectively. The pulse exposure duration was carried out 6 h in each event. The water quality conditions were maintained at water temperature 28 °C with pH 7.8. The used toxicokinetic parameter estimates were summarized in supplementary Table S1.

Table 1
Mechanistic expression of pulsed TK model and damage feedback TDM.

Bioaccumulation

$$\frac{dC(t)}{dt} = k_1 C_w(t) - k_2 C(t) \qquad \text{(T1-1)}$$

Cumulative damage

$$\frac{dD(t)}{dt} = k_k C(t) - k_r D(t) \qquad \text{(T1-2)}$$

Dynamics state of damage with hazard feedback loop

$$\frac{dD_H(t)}{dt} = k_s\left(D(t) - D_H(t)\right) + k_f\left(\frac{D_H^n(t)}{K^n + D_H^n(t)}\right)\cdot\left(D(t) - D_H(t)\right) - k_r D_H(t) \qquad \text{(T1-3)}$$

Steady state of damage with hazard feedback loop

$$k_s = \frac{D_H^n - k_r K^n D_H - (k_f + k_r) D_H^{n+1}}{(D_H - D)(D_H^n + K^n)} \qquad \text{(T1-4)}$$

Survival probability

$$S(t) = e^{-D_H(t)} \qquad \text{(T1-5)}$$

Adopted from Chen et al. (2012a,b).
Symbol meanings: $C(t)$ is the time-dependent Cu burden ($\mu g\, g^{-1}$ dry wt), $D(t)$ is the time-dependent damage (–),$D_H(t)$ is the time-dependent damage with hazard, $S(t)$ is the time-dependent survival probability (–), k_1 is the uptake rate constant ($L\, g^{-1}\, h^{-1}$), k_2 is the elimination rate constant (h^{-1}), k_k is the killing rate constant ($g\, \mu g^{-1}\, h^{-1}$), k_r is the recovery rate constant (h^{-1}), k_s is the external stimulus of Cu stressor (h^{-1}), k_f is the hazard feedback rate constant (h^{-1}), K is the effective D_H for 50% response for the feedback (–), and n is the Hill coefficient (–).

To determine the time- and Cu-dependent mortality of tilapia, Nussey et al. (1996) conducted the 96-h toxicity experiments using following Cu concentrations of 0, 1.0, 1.7, 1.8, 2.0, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 3.0, 3.5, and 4.0 $mg\, L^{-1}$ to observe the survival fish in each exposure tank. The time intervals of mortality measurement were 2, 4, 8, 12, 16, 24, 32, 48, 72, and 96 h. The water quality conditions were also maintained at water temperature 28 °C and pH 7.8.

2.2. Pulsed TK model and damage-feedback TDM

The TDM lays the foundations for predicting survival of aquatic organisms after exposed to sequential pulse and fluctuating patterns of chemical stressor. The dynamic equations for pulsed TK model and positive damage feedback TDM are listed in Table 1.

Briefly (Table 1), the first-order bioaccumulation model can be used to predict the body burden followed the exposure to sequential pulse Cu activities (Eq. (T1-1)). The time-dependent cumulative damage can be derived from the first-order damage accumulation model (Eq. (T1-2)). When a threshold for damage is exceeded, the time change of hazard (i.e., hazard rate) rises above zero, indicating the probability of the organisms suffering injury at a give time *t*. Chen et al. (2012a,b) proposed a simple system used to describe the positive damage feedback loop incorporating with the TDM. The damage feedback system consists of the reversible damage that can be converted between damage threshold (D_0) and damage with hazard (D_H) by a damage recovery rate constant k_r.

The process of threshold damage converting to reversible damage with hazard is regulated in two pathways (Eq. (T1-3)): (i) by an external stimulus of Cu stressor k_s and (ii) by a positive feedback with a Hill equation relationship between D_H generation and rate of generation of mode D_H. A steady-state relationship between D_H and external stimulus of metal stressor k_s can be obtained by setting $dD_H(t)/dt = 0$ (Eq. (T1-4)). The survival probability can be derived directly from the TDM and is given by an exponential function of damage with hazard (Eq. (T1-5)).