ABSTRACT

Fluctuation exposure of contaminant is ubiquitous in aquatic environments. Traditional standard laboratory toxicity tests were performed at constant exposure scenarios typically did not elucidate the short-term pulsed exposure toxicity to aquatic organisms. Little is known about copper (Cu) and arsenic (As) toxic effects with pulsed and fluctuation exposures on aquatic organisms. The purpose of this dissertation was to develop a quantitative systems-level approach utilizing toxicokinetics, toxicodynamics, bioavailability, and bioenergetics mechanisms to elucidate the ecophysiological response of tilapia (*Oreochromis mossambicus*) to fluctuating or sequential pulse Cu and As stresses. This study investigated the relationship among bioavailable metal, accumulative concentration and critical damage level induced growth toxicity for tilapia based on biotic ligand model (BLM), threshold damage model (TDM), and ontogenetic growth-based dynamic energy budgets in toxicology (DEBtox) model.

This study conducted the sequential pulsed Cu exposure bioassays on tilapia population to provide Cu acute/chronic toxicokinetics information. The 10-day and 28-day sequential pulsed Cu exposure experiments were conducted to obtain the bioconcentration factor (BCF) for tilapia population. This study linked bioavailability and bioaccumulation mechanisms to estimate the time and water chemistry dependent BCF. This also study analyzed the As exposure experimental data and pulsed Cu exposure bioassays of tilapia with growth inhibition response by using the proposed systems-level mechanistic model with periodic pulses and fluctuating exposures to simulate and compare the outputs. The ontogenetic growth-based DEBtox model was used to estimate growth coefficient (A_0) based on chronic growth bioassay, for assessing Cu and As chronic growth toxicities to tilapia.

The experimental results indicated that larvae had the highest BCF of 1116.10 mL g^{-1} that was greater than those of juveniles 225.50 mL g^{-1} and adults 94.00 mL g^{-1} in acute pulsed Cu exposure, whereas juveniles had the highest BCF 154.54 mL g^{-1} than that of adults 23.10 mL g^{-1} in chronic pulsed Cu exposure. Besides, tilapia had a higher Cu accumulation capacity than that of As (BCF=2.89 mL g^{-1}). Results also showed that BCF value depended significantly on water chemistry conditions and ions concentration. Moreover, BCF value decreased with the increasing of exposure duration. This study also found that tilapia in response to low-frequency Cu/As pulsed exposure had longer 50% safe probability time (ST50) than that of high-frequency pulsed exposure, whereas the longer ST50 was found in high frequency for Cu/As fluctuating exposure. The results indicated that the regulations were triggered between the pulsed intervals. The accumulation of the second Cu pulsed exposure was positively influenced by first Cu pulsed exposure that was consistent with the results of model simulation. The growth coefficients were estimated to be 0.029± 0.0015 $g^{1/4}$ d^{-1} (Mean±SE) for control and 0.019±0.0017 $g^{1/4}$ d^{-1} for pulsed Cu exposures in tilapia. The results indicated that growth coefficient depends positively on the exposure concentrations, revealing that Cu concentration inhibited growth energy and affected the growth of tilapia. The estimated dimensionless mass ratio revealed that sequential and fluctuating Cu exposure could increase tilapia energy acquisition than that of sequential and fluctuating As exposure for overcoming externally fluctuation-driven environments.

This study showed that the dynamics of physiological responses were dependent on the pulsed and fluctuating concentrations, duration, frequency, and different chemical exposure characters in tilapia. Moreover, the time and ions-dependent BCF provided a tool to assess the relationship between accumulation and toxic effect in the

field situation. We anticipated that this study could provide a completed quantitative systems-level dynamic approach for understating the ecophysiological response of aquatic organisms in response to metal stresses in the field situations. We also hoped that the proposed dynamics of ecophysiological response mechanistic model could successfully assess the long-term metal exposure risk for tilapia population in the field situation of metal exposure impact.

Keywords**:** Arsenic; Copper; Tilapia; Bioaccumulation; Bioavailability; Bioenergetics ; Pulsed/fluctuating exposure toxicity; Systems-level

中文摘要

水域環境普遍存在污染物的擾動現象。傳統標準實驗室毒性試驗皆於持續不變之暴露濃度情境下進行，但卻無法呈現短期脈衝暴露對水域生物之毒性效應。此外，銅與砷之脈衝與擾動暴露型態對水域生物所造成之效應甚少被研究。本論文之研究目的主要在於發展一量化系統層級法，利用毒理動力、毒理動態、生物可獲取率及生物能量機制解釋吳郭魚 (*Oreochromis mossambicus*)暴露於連續脈衝與擾動銅、砷濃度之生態生理反應。本研究以生物配體模式 (biotic ligand model, BLM)、閾值損害模式 (threshold damage model)及以毒理學之動態能量支出 (dynamic energy budgets in toxicology, DEBtox)為基礎之個體成長模式，探討可獲取的金屬、累積濃度及關鍵損害程度三者之相關性對成長毒性的影響。

本研究建構一吳郭魚暴露於脈衝銅濃度之生物試驗以提供急性與慢性暴露之毒理動力參數資訊。建構 10 天與 28 天之連續脈衝銅暴露實驗，以求得吳郭魚族群之生物濃縮因子 (bioconcentration factor, BCF)。亦結合生物可獲取率及生物累積機制，提供一方法推估隨時間及水化學而變化之生物濃縮因子。此外，本研究分析吳郭魚的成長抑制反應之砷暴露實驗數據及脈衝銅暴露生物試驗結果，運用本研究所提出之以系統層級機制模式，利用週期性脈衝及擾動暴露進行模擬與比較其模擬結果。再利用毒理學之動態能量支出為基礎之個體成長模式及慢性試驗數據推估成長係數 (A_0)，並評估吳郭魚對銅、砷之慢性成長毒性。

實驗結果顯示在急性脈衝銅暴露下，吳郭魚稚魚對銅之生物濃縮因子為 1116.10 mL g^{-1}，高於幼魚之 225.50 mL g^{-1} 及成魚之 94.00 mL g^{-1}。而在慢性脈衝銅暴露之 BCF 值則以幼魚的 154.54 mL g^{-1} 大於成魚之 23.10 mL g^{-1}。於結合生物可獲取率及生物累積機制之結果，顯示生物濃縮因子確實會受水化學條件、離子

濃度多寡而有所影響，且隨著暴露的時間愈長，其生物濃縮因子會愈小。此外，吳郭魚對銅的累積能力(BCF=94 mL g^{-1}) 高於對砷的累積能力(BCF=2.89 mL g^{-1})。本研究亦發現吳郭魚暴露於低頻率銅、砷脈衝暴露之 50%安全機率時間(ST50)大於高頻率暴露，而在擾動暴露則以 50%安全機率時間大於低頻率暴露。此結果顯示，吳郭魚會因不同的脈衝時間間距而啟動調節機制，且第二次脈衝銅暴露之累積程度確實受第一次脈衝銅暴露之影響，其結果均符合模式模擬之結果。而在吳郭魚控制組所推估之 A_0 為 0.029± 0.0015 $g^{1/4}$ d^{-1} (平均值±標準誤差)，而在脈衝銅暴露 A_0 為 0.019±0.0017 $g^{1/4}$ d^{-1}。此結果顯示成長係數確實會受暴露濃度所影響，表示銅濃度確實會抑制成長能量且影響吳郭魚之成長。由推估之無因次成長質量比例結果顯示在連續脈衝與擾動銅暴露下，吳郭魚會增加能量消耗大於連續脈衝與擾動砷暴露。

本研究顯示吳郭魚之生態生理反應動態會因脈衝及擾動濃度、持續時間、頻率及不同化學暴露特性而有所影響。再者，隨時間與離子濃度變化之生物濃縮因子可用以評估現地暴露狀況之毒性效應。因此，由本論文結果可知，運用量化系統層級動態法可了解水域生物在現地暴露狀況之生態生理反應。並期望所提出生態生理反應動態機制模式可成功地描述現地金屬暴露之影響狀態，而吳郭魚族群長期暴露於金屬之風險亦可精確地被評估。

關鍵字：砷；銅；吳郭魚；生物累積；生物可獲取率；生物能量；脈衝/擾動暴露毒性；系統層級