# A Developed Dynamic Network Model for Zebrafish Embryonic Abnormality Incidence Following Developmental Exposure to Tris(4-chlorophenyl) Methanol (TCPMOH)

The compound Tris(4-chlorophenyl) methanol (TCPMOH) is a contaminant of emerging concern due to its unknown etiology and recent detection in biological matrices including marine mammals and human breast milk. Here, we characterize the timing and incidence of embryonic defects following TCPMOH exposure in the zebrafish by applying the methodology of dynamic network models. Zebrafish embryos were exposed to a vehicle control (0.01% dimethyl sulfoxide), 0.5 μM, 1 μM, or 5 μM TCPMOH (n = 20-38 embryos per group) from 0-7 days post fertilization (dpf). Six morphological defects were assessed at 2-7 dpf: yolk edema, pericardial edema, spinal deformity, craniofacial malformation, swim bladder inflation, and mortality. Dynamic network models were developed for each exposure group to represent each abnormality (nodes) and their associations (links) over time. Network centrality analysis revealed TCPMOH exposed samples experienced a significant increase in abnormality co-occurrence when compared to controls. Yolk edema and pericardial edema are critical nodes with strong co-occurrence at early time points, inflicting the onset of further abnormalities later in the developmental process. Overall, this work not only characterizes the developmental toxicity of TCPMOH but also introduces a dynamic network model to assess developmental toxicology integrating structural and temporal features with concentration response.

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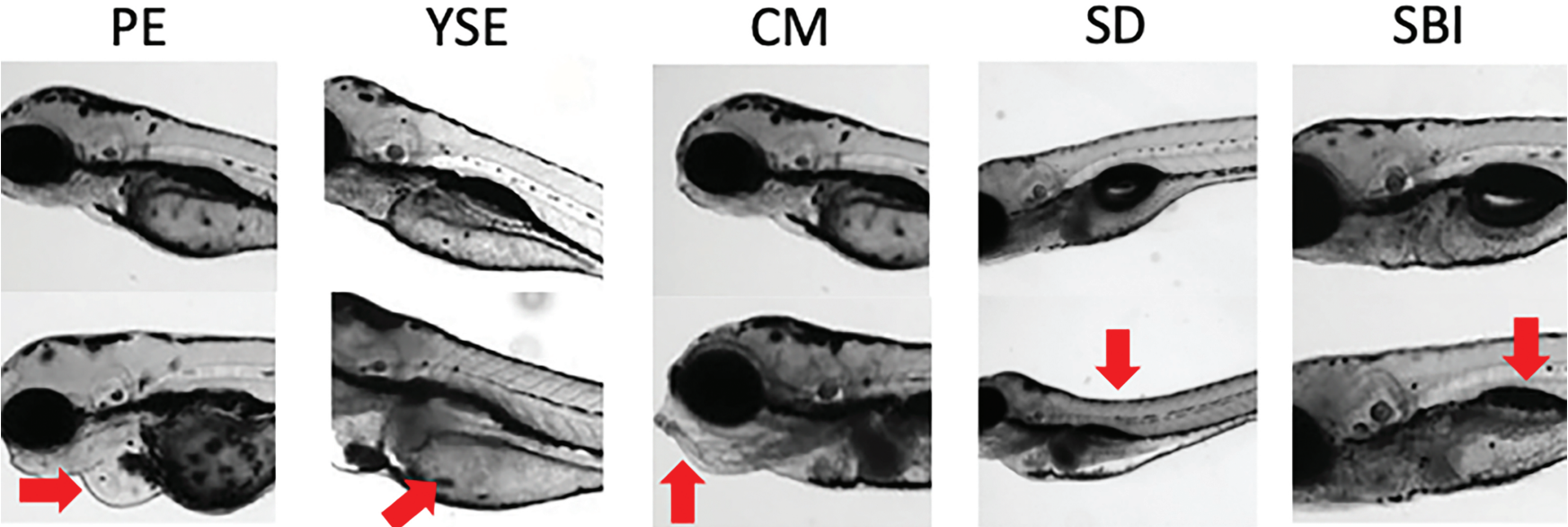
Observed developmental abnormalities in zebrafish exposed to TCPMOH: pericardial edema (PE), yolk sac edema (YSE), cranial malformation (CM), spinal deformity (SD), swim bladder inflation (SBI), and mortality (M, not pictured). Control (top photo) and abnormal zebrafish (bottom photo) are shown with the red arrow pointing directly to the defect.
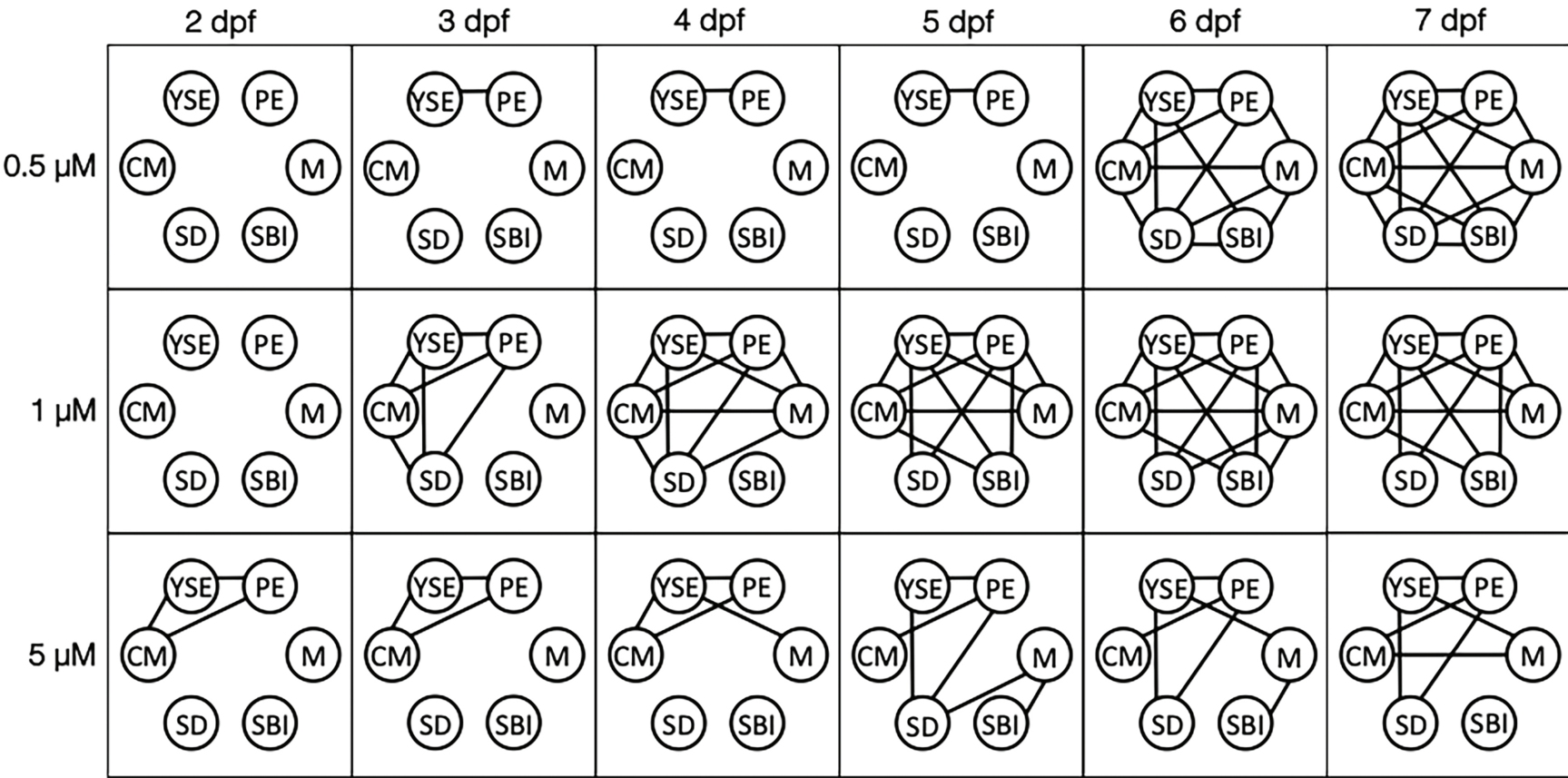
A dynamic network model for abnormality co-occurrence in differing exposure levels of TCPMOH over time. The network represents the abnormalities (nodes) and the time-dependent associations between them (links).