Zebrafish as a Sustainable Animal Model in Biomedical Research

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The global scientific community faces a constant challenge: advancing biomedical research responsibly, affordably, and sustainably, while reducing costs and environmental impact. While traditional mammalian models have driven major discoveries, they also come with ethical constraints, high maintenance costs, long generation times, and substantial environmental demands involving space, water, energy, and feed. In contrast, the zebrafish (Danio rerio) has emerged as an excellent, low-cost, high-throughput research model that unites accessibility, versatility, and sustainability.

Why Zebrafish Are a Sustainable Model in Biomedical Research?

Affordability: Zebrafish require compact aquatic systems, low-volume water usage, and minimal feed, significantly reducing the environmental footprint compared to mammalian facilities.

High Fecundity and rapid development: A single pair of zebrafish can lay up to 200-300 eggs per week. Zebrafish embryos develop rapidly, with major organ systems forming within 24-48 hours post-fertilization, allowing for rapid experimental turnaround.

High Genetic Homology: Zebrafish share 70% of human genes, and 84% of disease-associated genes have zebrafish orthologs. Zebrafish possess a remarkable regenerative capacity and share major organs with humans, including the heart, liver, and kidneys.

Transparency Advantage: Zebrafish larvae are nearly transparent, enabling non-invasive, real-time microscopy of organ development, blood flow, and drug effects.

Transgenic Lines: Fluorescent transgenic lines like Tg(fli1:EGFP) for vessels, Tg(myl7:EGFP) for heart cells, and Tg(GATA1:dsRed) for erythrocytes, leveraged with transparency, enable high-resolution, non-invasive in vivo imaging of tissue dynamics and gene activity.

Zebrafish and the 3Rs for Ethical and Sustainable Approach: The zebrafish model organism aligns with the 3Rs principle (Reduce, Refine, Replace) and contributes to more ethical and sustainable research practices.

Reduction: Zebrafish larvae up to 5 days post-fertilization are exempted from ethical regulation for vertebrate models. This exemption reduces reliance on mammalian systems, lowers resource demands, and supports more sustainable research practices.

Refinement: Zebrafish offer high-throughput data collection, reducing the number of animals required per study.

Replacement: Zebrafish can substitute mammalian models in early-phase screenings, minimizing ecological and ethical impact.

Zebrafish Animal Model in Biomedical Research

At IIT Hyderabad, our lab employs zebrafish as a sustainable vertebrate model for research spanning mental health, cancer, toxicology, and drug efficacy. Our work integrates innovative in-house tools and techniques, further improving affordability and accessibility.

Mental Health Disorders

Despite their evolutionary distance, zebrafish possess conserved neuroanatomical and neurochemical pathways (including serotonin, dopamine, and GABA systems) relevant to human neuropsychiatric conditions. At IIT Hyderabad, our lab utilizes the in-house developed (in collaboration) open-source low-cost ZebraTrack [1] method to assess anxiety behaviour in zebrafish. This aligns strongly with sustainability goals by reducing reliance on expensive tracking systems.

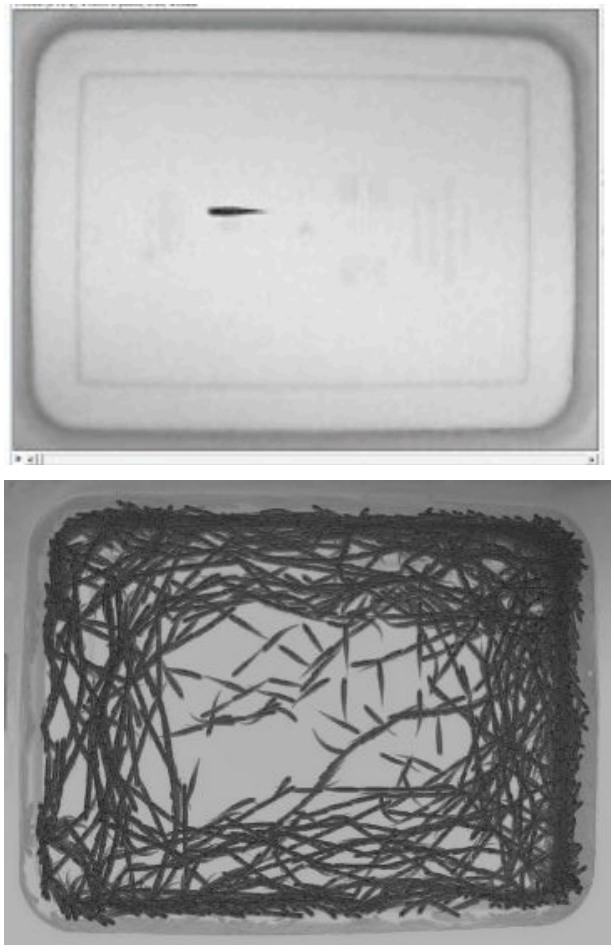

Fig 1: Swimming trajectory of zebrafish in the open-field test tank, analyzed using the ZebraTrack method [1]. The trajectory (path followed by zebrafish overtime) illustrates locomotor behaviour used to assess neurotoxicity

Cancer Xenografts

Zebrafish larvae lack a fully developed adaptive immune system, allowing non-rejected transplantation of human cancer cells. This creates a rapid and visually accessible system for studying tumor growth, angiogenesis, metastasis, and therapeutic response.

Our group has successfully established a zebrafish breast cancer xenograft model, enabling real-time visualization of tumor progression and screening of anti-cancer compounds [2].

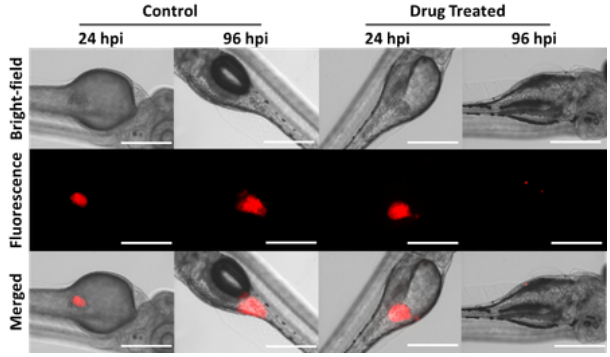

Fig 2: Zebrafish breast cancer xenograft model for tumor growth, metastasis and drug efficacy research. Red colour represents fluorescently labelled breast cancer cells injected into the zebrafish larvae. Drug treatment could eliminate cancer in vivo. hpi= hours post injection. Figure reproduced from [2].

Toxicology and Drug Efficacy Screening

Zebrafish enable multi-well plate-based drug screening, with embryos absorbing test compounds directly from water. This bridges the gap between cell culture and mammalian models while dramatically reducing material requirements. We use zebrafish larvae to evaluate cardiotoxicity, neurotoxicity, and systemic toxicity of drugs, herbicides, and environmental contaminants [3].

Our lab has developed ZebraPace in collaboration, an open-source method for accurate quantification of cardiac rhythm in untethered zebrafish larvae [4].

Conclusion

Zebrafish have become a cornerstone of modern biomedical research due to their genetic relevance, rapid growth, transparency, and experimental versatility. Their low environmental footprint, compatibility with the 3Rs, and high-throughput capabilities make them a sustainable alternative to traditional mammalian models. At IIT Hyderabad, the integration of zebrafish models across disciplines, from toxicology and neuroscience to cancer research, demonstrates our commitment to ethical, affordable, and environmentally responsible scientific advancement.

References

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3. Pullaguri, N., et al. (2021). Triclosan affects motor function in zebrafish larva by inhibiting ache and syn2a genes. Chemosphere, 266, 128930.
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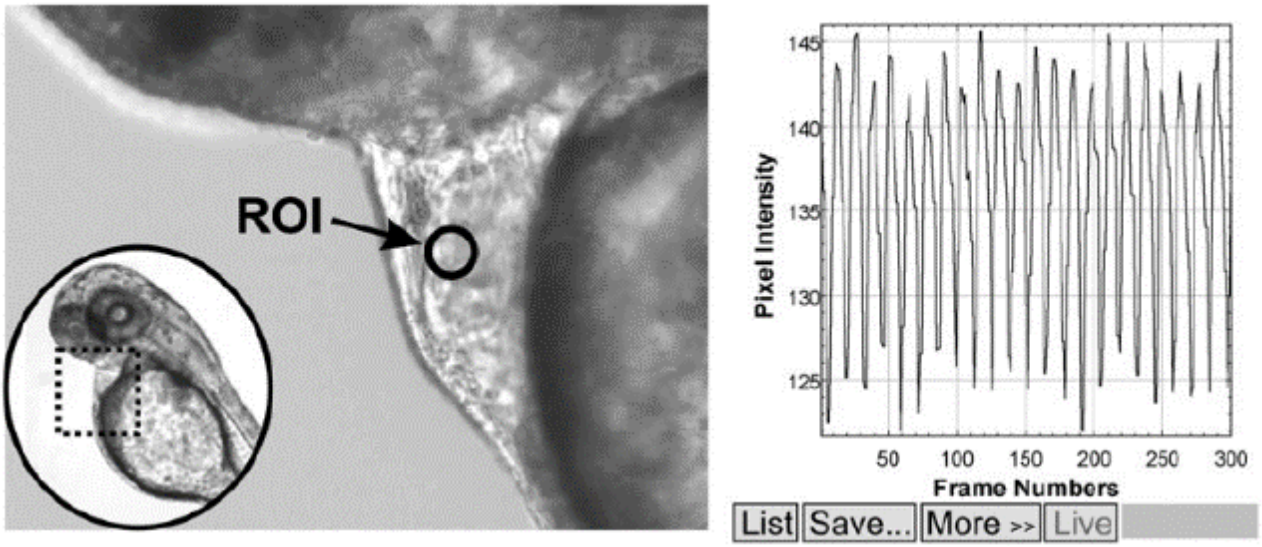

Fig 3: Heartbeat analysis in zebrafish larvae using the ZebraPace method for cardiotoxicity assessment. Figure reproduced from [4].

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