

Conditional Machine Learning Model for Scalable Landmark Detection in Comparative Morphological Imaging of Medaka Inbred Lines

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Genotype–phenotype mapping relies on precise quantification of anatomical shape. The Medaka Inbred Kiyosu–Karlsruhe (MIKK) panel of 80 fully sequenced isogenic inbred lines offers a powerful resource for systematic genetic studies. High-throughput synchrotron microtomography generates high-resolution 3D volumes of hundreds of medaka fish specimens, but converting these multi-gigabyte volumes into quantitative morphological traits remains challenging. Traditional dense 3D convolutional networks demand excessive GPU memory and scale poorly with image size and target landmark count, limiting large-scale comparative studies across inbred lines.

We propose a hybrid conditional framework that combines reinforcement learning for efficient coarse landmark localization with a convolutional network for high-precision refinement. A conditional reinforcement learning agent navigates large volumes using local 3D observations and learns a landmark-conditioned policy with a single shared model across all landmarks, ensuring a small memory footprint. This agent produces coarse landmark positions, which are subsequently refined by a conditional 3D convolutional network operating on a high-resolution region of interest. The refinement network outputs localized heatmaps, enabling subvoxel accuracy. The conditional design allows the framework to scale to an arbitrary number of landmarks and naturally leverage partially annotated training data.

We applied our model to 3D volumes of medaka fish with up to 49 anatomical landmarks per specimen. The method achieves localization accuracy comparable to inter-annotator variability while drastically reducing GPU memory consumption relative to dense 3D baselines. This efficiency makes large-scale processing of the hundreds of specimens within the MIKK panel feasible on standard hardware. The automatically detected landmarks enable systematic cross-line comparisons of morphological distances, angles, and shape configurations, supporting the design of targeted F2 crosses guided by trait patterns.