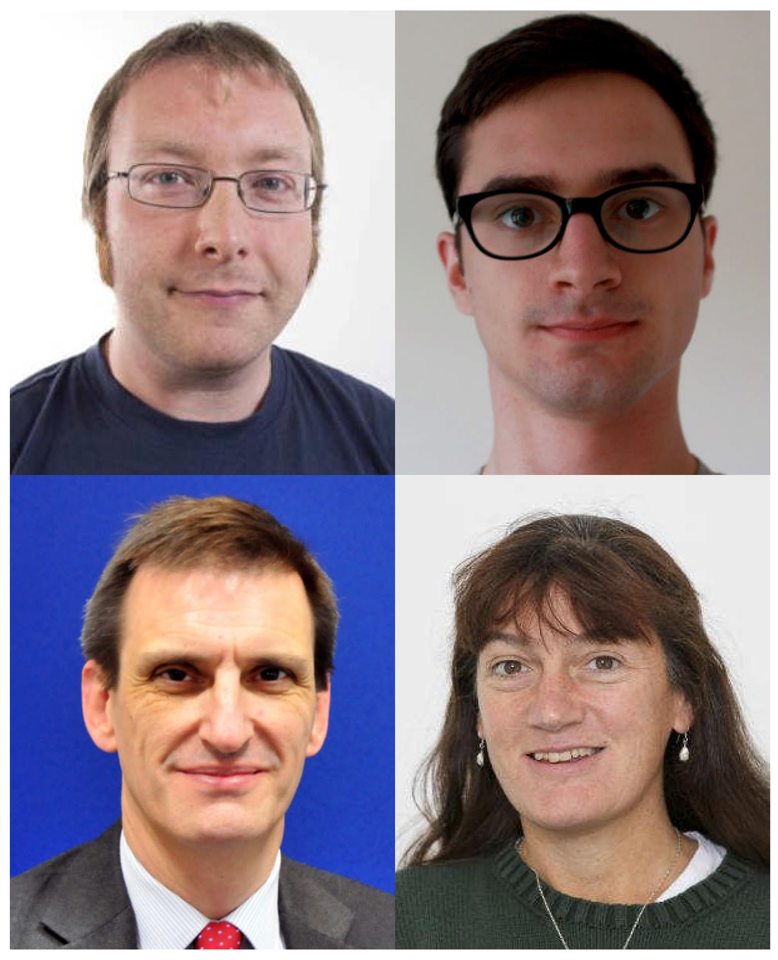
Centre for Chronic Diseases & Disorders (C_2D_2)



Zebrafish: A New Vertebrate Model of Parkinson’s Disease

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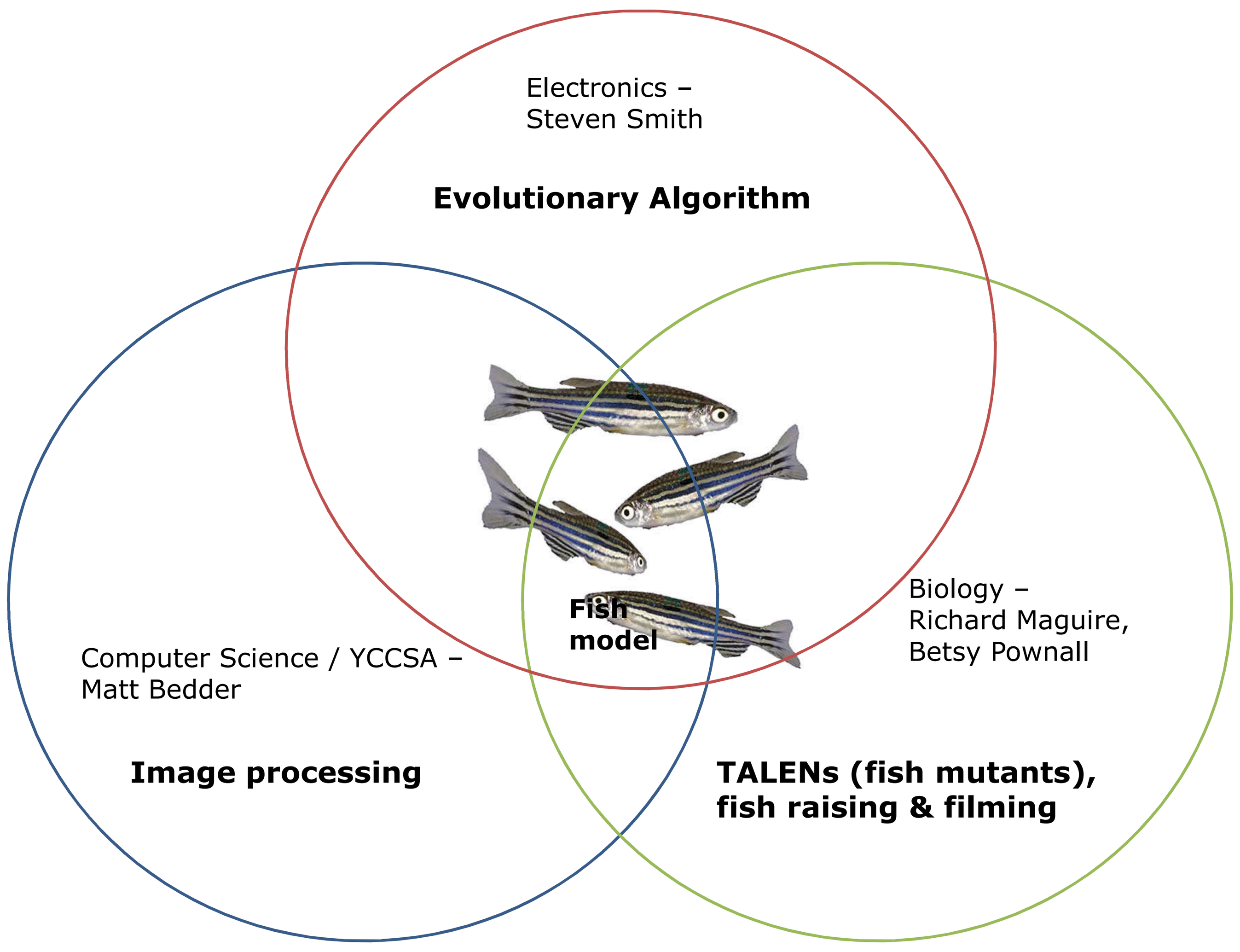
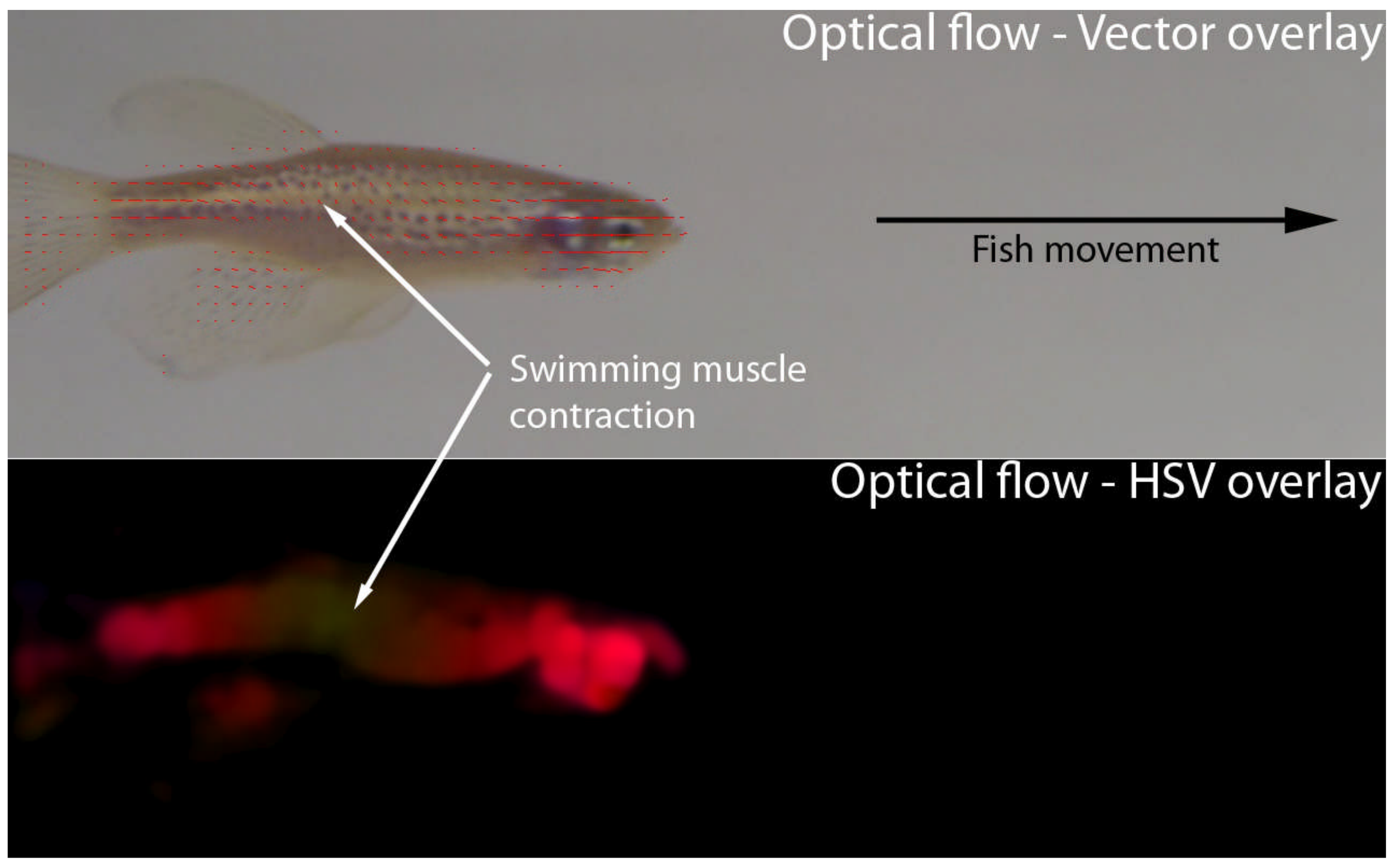


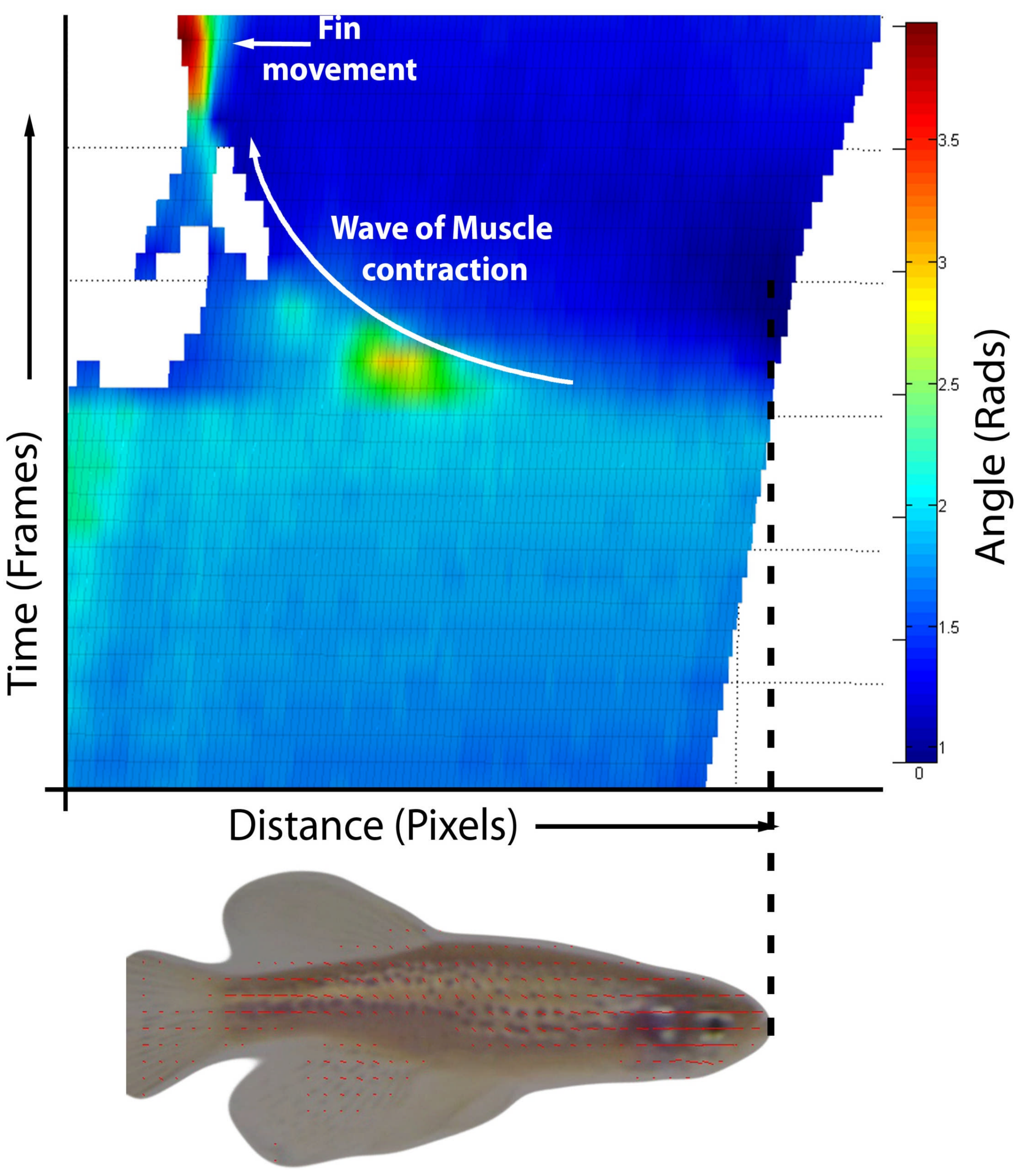
1. A Multidisciplinary approach to develop Parkinson’s Disease models

This project is a collaboration between members of three University departments and YCCSA, which involves the application of novel biological and computational techniques to the development of a fish model of Parkinson’s Disease. Data from non-invasive filming techniques will be used to train an evolutionary algorithm to precisely define movement differences between mutant and non-mutant fish.



2. Using optical flow to track movement

Optical flow refers to the pattern of apparent motion of objects (in This case a fish) in a visual scene. Here you can see that there is a change in direction and magnitude of the optical flow, as represented by the vector overlay above, where direction is expressed by the orientation of the red lines and magnitude by their length (top). This can also be represented more simply by a colour map (bottom) where higher magnitude movement maps to a more intense colour and direction maps to the red/green hue.

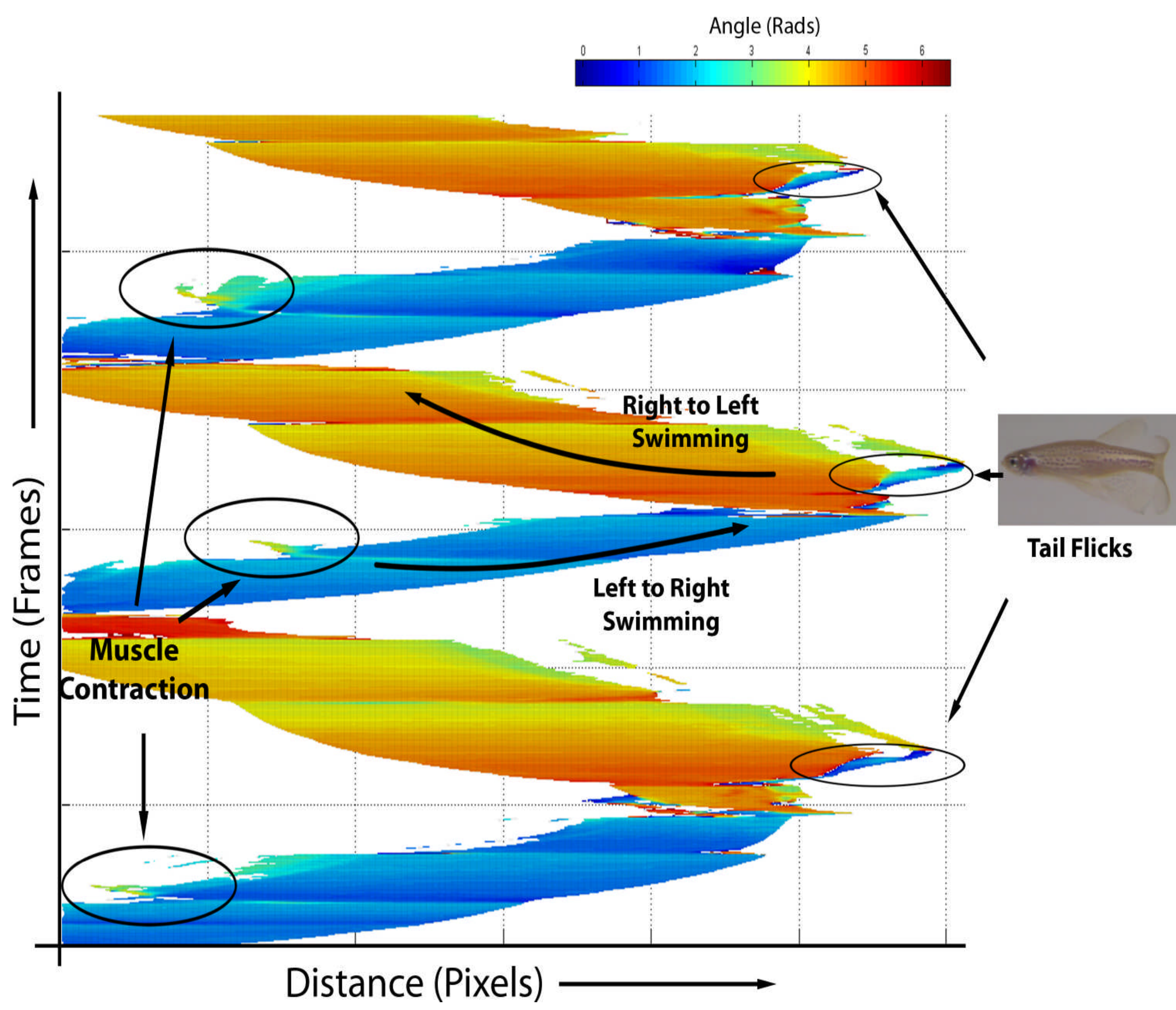


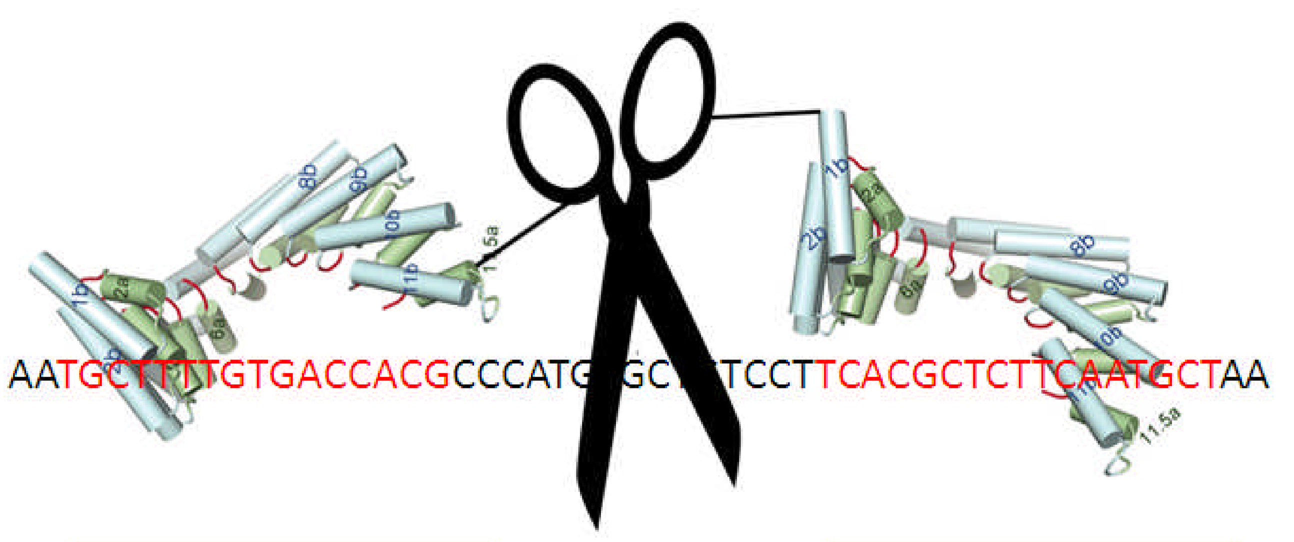
3. Optical flow over time produces useful movement data

When optical flow information from concurrent frames is overlaid, useful data is generated which can potentially be used to train the evolutionary algorithm and determine differences in movement characteristics between fish populations.

LEFT
Changes in flow vector angles over time corresponds very well to the progression of muscle contraction down the body of a fish.

RIGHT
Flow vector angles can be plotted over several phases of fish movement and distinct features can be picked out which correspond to real swimming behaviours. It will be important to collect many such profiles in order to train the Evolutionary Algorithm.



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AATGCTTTTGTGACCACGCCCATGTGCTGTCCTTCACGCTCTTCAATGCTAA   WT
AATGCTTTTGTGACCA--------------------CGCTCTTCAATGCTAA   Δ20 [2x]
AATGCTTTTGTGACCACG-----------TCCTTCACGCTCTTCAATGCTAA   Δ11
AATGCTTTTGTGACCACGCCCA----------TTCACGCTCTTCAATGCTAA   Δ10
AATGCTTTTGTGACCACGCCCATG--------TTCACGCTCTTCAATGCTAA   Δ8
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4. TALENs provide a novel mechanism to cause targeted, heritable mutations in genes implicated in Parkinson’s Disease at will

TALENS (TAL Effector like Nucleases) comprise of a modular, customisable DNA binding domain (Stick model, left) fused to the nuclease domain of Fok1 (scissors, left). When introduced to cells, they bind specifically to target sequences (red and yellow highlights) and induce double strand breaks (red dashed regions indicated).

We are currently using TALENs directed against the early onset Parkinson’s Disease genes *Parkin2* and *Pink1* which are highly conserved in the Zebrafish. We hope to have test fish by the end of the year. In the mean time we intend to calibrate the evolutionary algorithm on different populations of wild type fish.

The University of York
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