Faculty and PostDoc, Medical, Biomedical and Health Sciences

Computational modeling of motile cilia generated cerebral flow dynamics in zebrafish embryo

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BACKGROUND

- Motile cilia are hair-like microscopic structures which move the fluids along the epithelial surfaces.
- Cilia cover a wide range of regions in the nervous system, such as the nasal cavity, central canal of spinal cord, and brain ventricles.
- Motile cilia-driven cerebrospinal fluid (CSF) flow in the brain ventricles has an important role in brain development.
- Embryos lacking motile cilia develop neurological defects due to altered CSF flow.

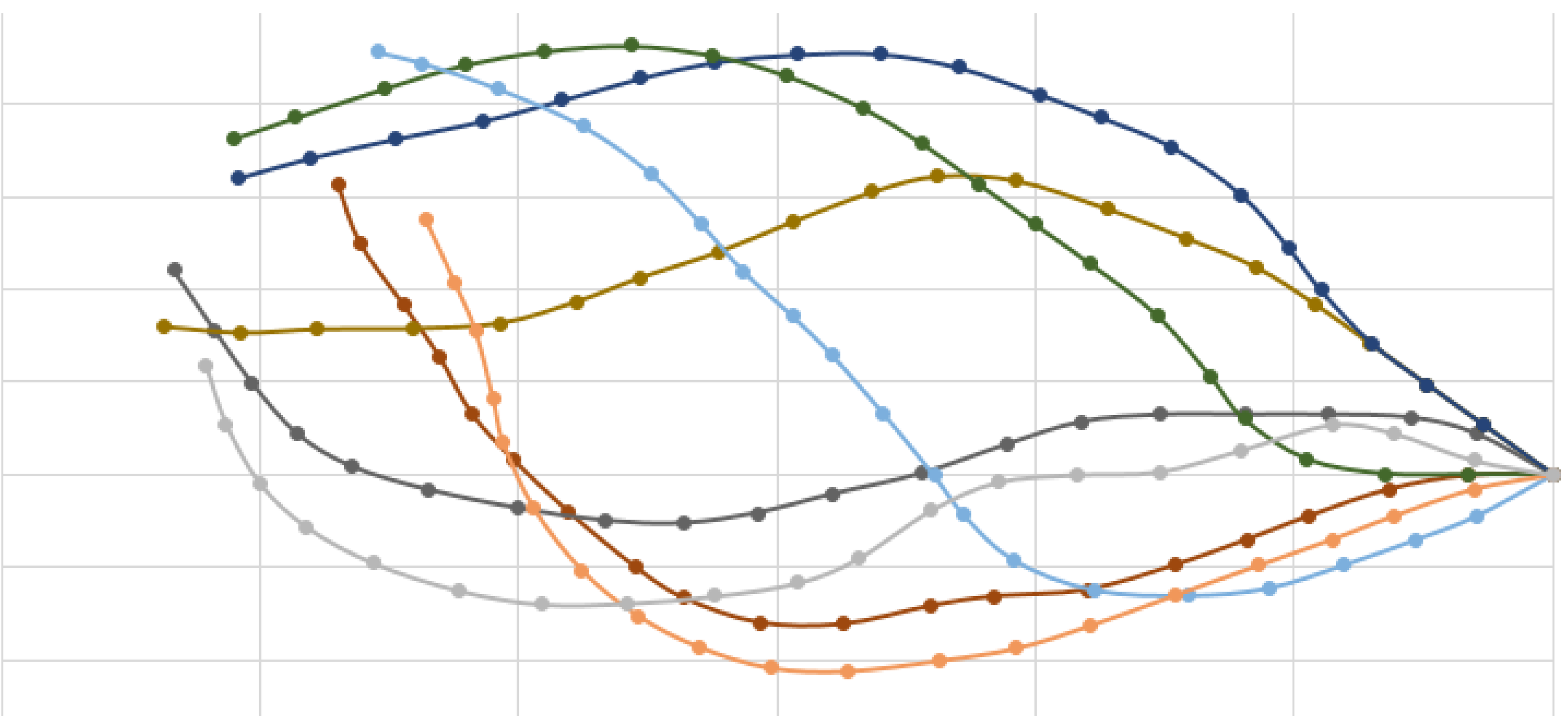
OBJECTIVE

To investigate the effect of motile-cilia motion on the altered CSF flow, and to understand the role of CSF flow in the brain development and physiology.

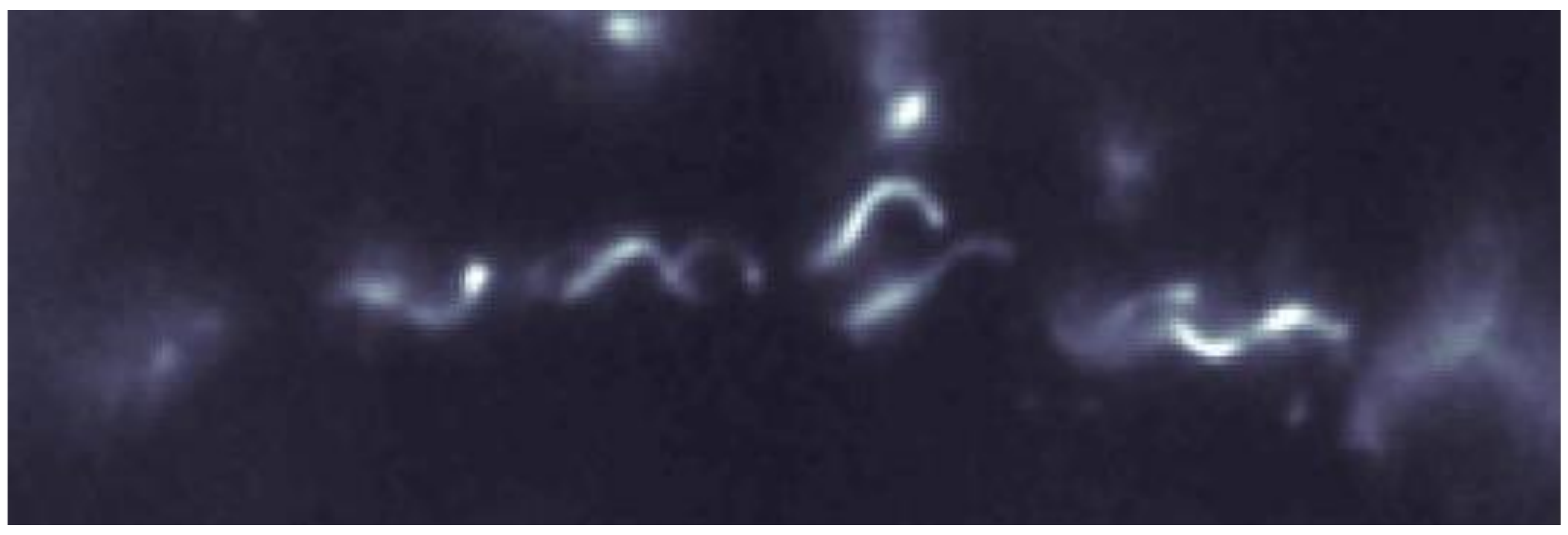
METHODOLOGY

Computational fluid dynamics simulations

- Mathematical solution is approximated with numerical techniques by following the steps:
- Generation of 2-dimensional simplified brain ventricle flow domain
- Discretization of the problem domain into finite elements (Meshing)
- Defining a full cycle of motile-cilia motion using the time-lapse microscopic movies showing movements of a fluorescently labeled motile-cilia in a zebrafish embryo (48-hour post-fertilization)



Motile-cilia motion steps during one full cycle



Motile-cilia in the brain ventricle of 48 hpf zebrafish embryo

- Post-processing the results after 30 cycles of motile-cilia motion
- The governing equations in fluid domain:

$$\rho_f \frac{\partial \mathbf{v}}{\partial t} + \rho_f (\mathbf{v} - \mathbf{w}) \cdot \nabla \mathbf{v} - \nabla \cdot \boldsymbol{\tau}_f = \mathbf{f}_f^{\mathrm{B}}$$

$$\nabla \cdot \mathbf{v} = 0$$

ρ_f: Mass density of fluid, $\mathbf{v}$: Fluid velocity vector, t: Time

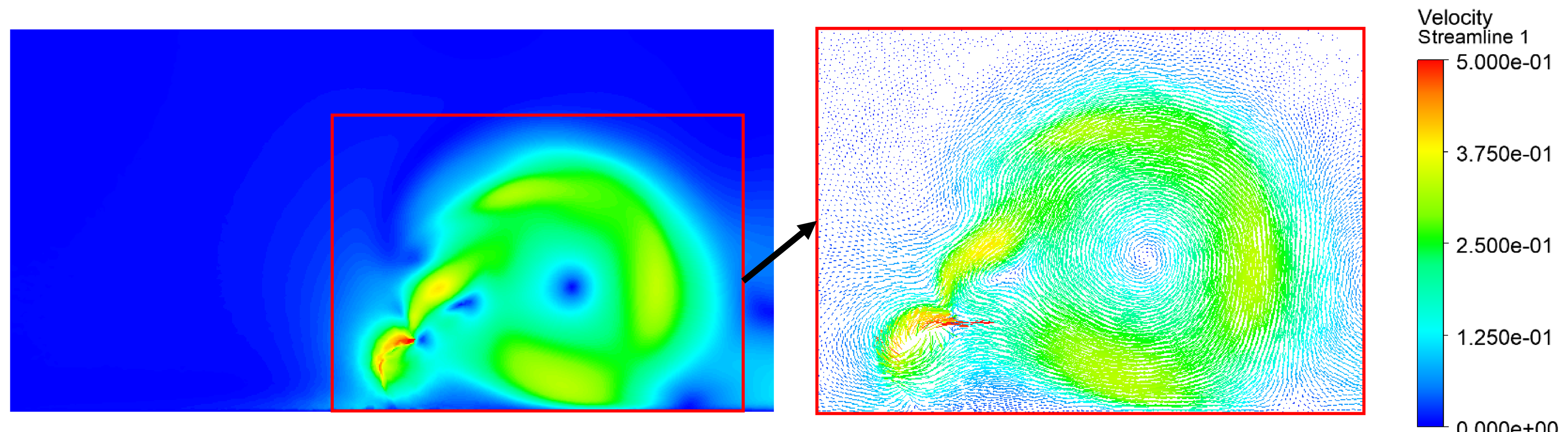
$\mathbf{w}$: Velocity of the fluid domain (i.e. moving coordinate velocity)

$\boldsymbol{\tau}_f$: Fluid stress tensor, $\mathbf{f}_f^{\mathrm{B}}$: Body forces

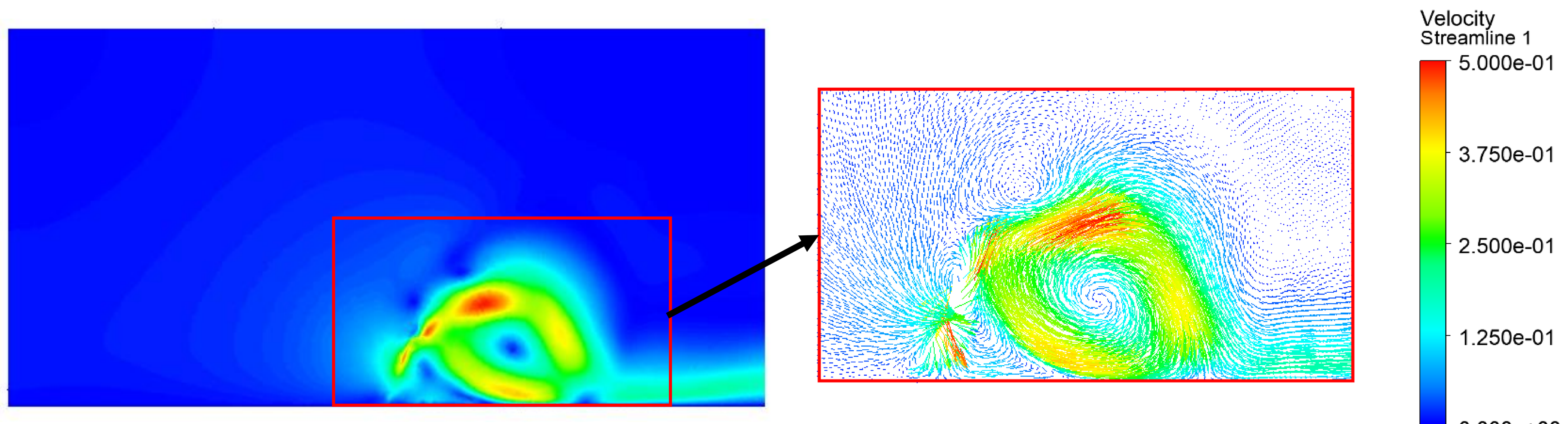
- CSF flow velocities are determined in the entire flow domain.
- The effects on the generated flow are elucidated by investigating the cilia beating angle, multiple cilia formations, and phase difference between different ciliary beats.

RESULTS

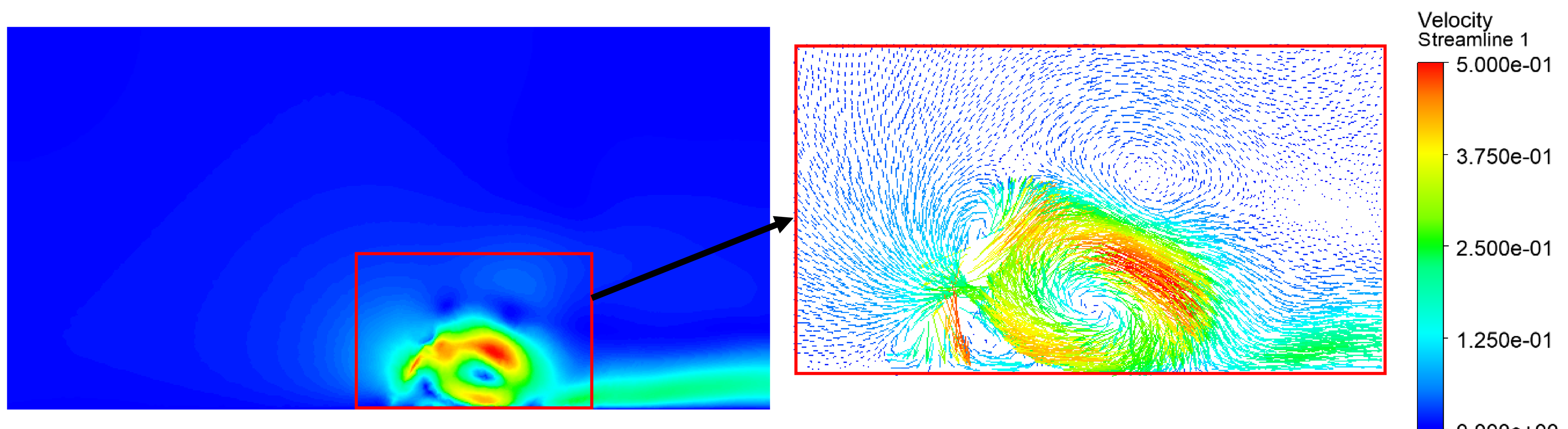
Cilia with 90° angle *Cilia with 60° angle* *Multiple cilia with 60° angle*



90° angle between the cilia and brain ventricle wall

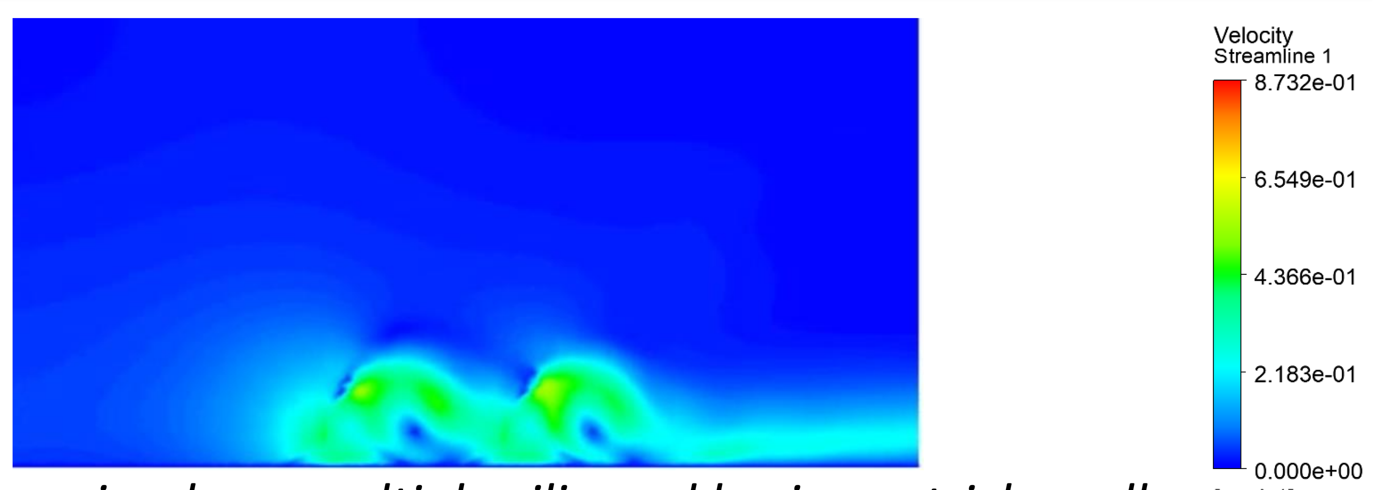


70° angle between the cilia and brain ventricle wall

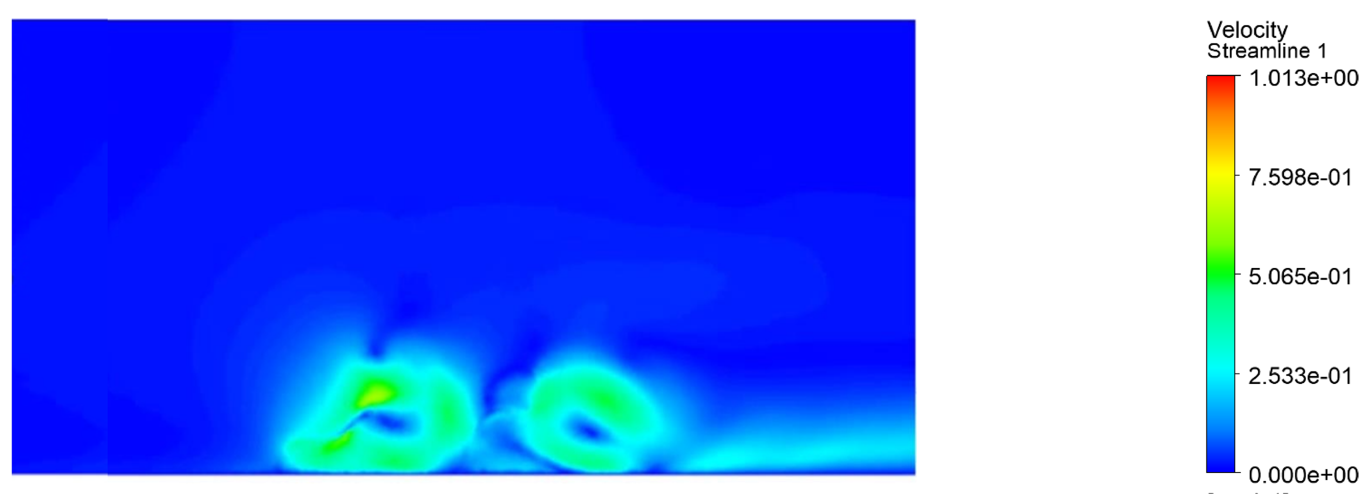


60° angle between the cilia and brain ventricle wall

- Ciliary beating generated a directional flow in the form of a circulating vortex.
- The angle of ciliary beating significantly affected the flow velocity.
- As the angle between the wall and cilia decreases, CSF flow achieves higher velocities (8.4% difference between 90° and 60° cilia angles).



60° angle between in-phase multiple cilia and brain ventricle wall



60° angle between out-of-phase multiple cilia and brain ventricle wall

- Multiple cilia formations increased the flow velocity but the significance of multiple cilia is not as critical as the beating angle.
- Interestingly, phase difference between the multiple cilia beats increased the directional flow velocity (16.0% difference with in-phase cilia beating).

CONCLUSION

Motile-cilia generated flow dynamics are investigated, and it is concluded that out-of-phase multiple ciliary beating is the optimum form of beating in order to generate a directional flow.