

# Large Amplitude, Short Wave Peristalsis and Its Implications for Transport

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## ABSTRACT

Valveless, tubular pumps are widespread in the animal kingdom, but the mechanism by which these pumps generate fluid flow are often in dispute. Where the pumping mechanism of many organs was once described as peristalsis, other mechanisms, such as dynamic suction pumping, have been suggested as possible alternative mechanisms. Peristalsis is often evaluated using criteria established in a technical definition for mechanical pumps, but this definition is based on a small-amplitude, long-wave approximation which biological pumps often violate. In this study, we use a direct numerical simulation of large-amplitude, short-wave peristalsis to investigate the relationships between fluid flow, compression frequency, compression wave speed, and tube occlusion. We also explore how the flows produced differ from the criteria outlined in the technical definition of peristalsis. We find that many of the technical criteria are violated by our model: fluid flow speeds produced by peristalsis are greater than the speeds of the compression wave; fluid flow is pulsatile; and flow speed have a non-linear relationship with compression frequency when compression wave speed is held constant. We suggest that the technical definition is inappropriate for evaluating peristalsis as a pumping mechanism for biological pumps because they too frequently violate the assumptions inherent in these criteria. Instead, we recommend that a simpler, more inclusive definition be used for assessing peristalsis as a pumping mechanism based on the presence of non-stationary compression sites that propagate uni-directionally along a tube without the need for a structurally fixed flow direction.

Keywords: Peristalsis, embryonic hearts, fluid dynamics

## 1 INTRODUCTION

Tubular pumps are found across the animal kingdom in all stages of development (*e.g.* Griffiths et al, 1987; Gashev, 2002; Xavier-Neto et al, 2007; Lee and Socha, 2009; Glenn et al, 2010; Xavier-Neto et al, 2010; Krenn, 2010; Greenlee et al, 2013; Harrison et al, 2013a). In all vertebrate embryos, the heart first forms as a valveless tubular pump (*e.g.* Taber, 2001). Similarly, the hearts of many non-vertebrate chordates such as tunicates are also valveless, tubular pumps (Anderson, 1968; Kalk, 1970; Glenn et al, 2010; Waldrop and Miller, 2015). In the last 10 years, the mechanism of pumping in tubular hearts and other tubular pumps has been described as either peristalsis or dynamic suction pumping (Forouhar et al, 2006; Taber et al, 2007; Männer et al, 2010; Maes et al, 2011).

For the case of peristalsis, a wave of active contraction propagates down the length of the tube. Since the advent of mechanical peristaltic pumps (*i.e.*, roller pumps), the technical definition of a peristaltic pump has been refined to include these characteristics (summarized in Männer et al (2010)):

1. Peristaltic pumps are positive-displacement pumps, which displace a fixed volume to create fluid flow.
2. Peristaltic pumps have non-stationary compression sites, *i.e.*, waves of compression that uni-directionally propagate down a flexible tube.
3. Peristaltic pumps produce continuous flow.
4. There are no structurally fixed directions of flow (*e.g.*, there are no one-way valves), and the direction of flow is determined by the direction of the compression wave.

- 28 5. Flow velocity is equivalent to the speed of the compression wave. Peak flow velocity does not  
29 exceed the speed of the compression wave.
- 30 6. There is a linear relationship between the frequency of the compression wave and flow rate it  
31 produces.

32 The principles of the technical definition are based upon a body of analytical work using small-amplitude  
33 and/or long-wave approximations of peristaltic pumping where nonlinear effects, such as inertia and  
34 large flows in the radial direction, are small (Jaffrin and Shapiro, 1971; Hanin, 1968; Shapiro et al, 1969;  
35 Fung and Yih, 1968). These results may not apply to cases when inertia is non-negligible or where the  
36 compression amplitude is not small relative to the diameter or the wavelength. These nonlinear cases do,  
37 however, characterize many biological pumps (Santhanakrishnan and Miller, 2011).

38 There are, however, some numerical and analytic results available for large amplitude and/or short  
39 wavelength peristalsis. Childress (2009) showed analytically for large occlusion ratios and long wave  
40 lengths that the peak flow velocity can exceed the peristaltic wave speed. Pozrikidis (1987) modeled  
41 peristalsis for relatively small wavelengths in a Stokes fluid. He found that peak flow velocities are nearly  
42 twice the wave speed for an 80% occlusion of the tube. Large amplitude, short wave peristalsis has also  
43 been studied numerically for Stokesian viscous and viscoelastic fluids. Teran et al (2008) simulated up to  
44 50% occlusion and reported only mean flow rates for viscous and viscoelastic fluids. Aranda et al (2011)  
45 simulated high amplitude peristaltic pumping in a three-dimensional tube with a phase-shifted asymmetry.  
46 The mean flow rate approached the wave speed for full occlusion, implying that the peak speeds are higher  
47 than the wave speed given the large spatial and temporal variations in the flow. Ceniceros and Fisher  
48 (2012) also simulated viscoelastic fluids at high occlusion ratios but also only reported mean flow rates.  
49 For Newtonian fluids in nearly occluded tubes, mean flow rates approached the wave speed. Given the  
50 large spatial variations in flow as evidenced by the given vorticity plots, it is likely that peak flow speeds  
51 were much higher than the wave speed.

52 In contrast, dynamic suction pumping is defined by an isolated region of active contraction that is  
53 asymmetrically located in a section of flexible tube connected to relatively stiffer inflow and outflow  
54 tracts (Liebau, 1954, 1957, 1955). Passive elastic traveling waves emanate from the active contraction  
55 site, and these waves drive flow. Analytical models (Auerbach et al, 2004; Bringley et al, 2008), physical  
56 experiments (Hickerson et al, 2005a; Bringley et al, 2008), and numerical simulations (Jung and Peskin,  
57 2000; Jung et al, 2008; Baird et al, 2014) support that this pumping mechanism can effectively transport  
58 fluid under certain conditions. Furthermore, these pumps are characterized by a nonlinear frequency-flow  
59 relationship, reversals in flow directions, and flow speeds higher than the wave speed.

60 Based on the technical definition of peristalsis, Forouhar *et al.* (2006) make the case that the zebrafish  
61 embryonic heart is not a peristaltic pump by observing the kinematics of heart compression and blood  
62 flow *in vivo*. They found these observations violated some of the principles that underpin peristalsis,  
63 specifically: they observed bidirectional compression and reflection waves of the heart muscle and imply  
64 that activation of the muscle was limited to one site (#2 and #3), the flow velocity inside the heart exceeded  
65 the compression wave speed (#5), and there was a non-linear relationship between blood flow speed  
66 and the frequency of heart compressions (#6). As a result of these observations, Forouhar et al (2006)  
67 reject peristalsis and suggest that the fluid dynamics of the embryonic vertebrate heart share more of the  
68 properties of dynamic suction pumping than peristalsis (a localized site of active compression is placed  
69 off-center, and the resulting traveling waves are passive elastic).

70 Since the publication of this paper nearly 8 years ago, some researchers have speculated that other  
71 biological pumps drive blood and other fluids using dynamic suction pumping (Davidson, 2007; Vogel,  
72 2007; Harrison et al, 2013b). Other researchers continue to describe tubular pumping in the embryonic  
73 heart as peristalsis (Christoffels and Moorman, 2009; Postma et al, 2008; Taber et al, 2007). Some of these  
74 tubular pumps, like tunicate hearts and many embryonic hearts, violate the low-amplitude, long-wave  
75 assumptions of the technical definition of peristalsis. In many of these cases, the compression wave almost  
76 completely occludes the tube, action potentials are known to propagate the length of the entire tube by  
77 activating helically wound muscle fibers (Anderson, 1968; Kalk, 1970), and the width of the tube is not  
78 significantly longer than its length. Furthermore, these pumps are often at a scale where neither inertial  
79 nor viscous effects can be neglected.

80 In this paper, we use direct numerical simulation of the fully coupled fluid-structure interaction  
81 problem to quantify the flows generated by large-amplitude, short-wave peristalsis. We then evaluate

82 which aspects of the technical definition of peristalsis a large-amplitude, short-wave peristaltic pump can  
 83 fulfill. The simulations were done using the immersed boundary method (Peskin, 2002). The peristaltic  
 84 wave was prescribed as a traveling sine wave. The length of the tube was four times the diameter, and the  
 85 region of prescribed motion was centered in the middle of the tube. The ends of the elastic section were  
 86 allowed to bend as determined by the coupling between the fluid and the elastic tube. We quantify peak  
 87 and average fluid speeds downstream of the compression region, the pressure at the inflow and outflow  
 88 points of the compression tube, and flow speeds at a point within the compression region.

## 89 2 METHODS

### 90 2.1 The Immersed Boundary Method

91 The modeling and numerical simulations of peristalsis were conducted with the immersed boundary  
 92 method (Peskin, 2002) using the library IBAMR (Griffith, 2014). The IB method can be used either  
 93 to simulate a boundary moving with a prescribed motion or for solving for the motion based on the  
 94 interaction of the fluid with an elastic boundary. The following outline describes the two-dimensional  
 95 formulation of the immersed boundary method, but the three-dimensional extension is straightforward.  
 96 For a full review of the method, see Peskin (2002). The equations of fluid motion are given by the  
 97 Navier–Stokes equations:

$$\rho(\mathbf{u}_t(\mathbf{x}, t) + \mathbf{u}(\mathbf{x}, t) \cdot \nabla \mathbf{u}(\mathbf{x}, t)) = -\nabla p(\mathbf{x}, t) + \mu \nabla^2 \mathbf{u}(\mathbf{x}, t) + \mathbf{F}(\mathbf{x}, t) \quad (1)$$

$$\nabla \cdot \mathbf{u}(\mathbf{x}, t) = 0 \quad (2)$$

98 where  $\mathbf{u}(\mathbf{x}, t)$  is the fluid velocity,  $p(\mathbf{x}, t)$  is the pressure,  $\mathbf{F}(\mathbf{x}, t)$  is the force per unit area applied to the  
 99 fluid by the immersed boundary,  $\rho$  is the density of the fluid, and  $\mu$  is the dynamic viscosity of the fluid.  
 100 The independent variables are the time  $t$  and the position  $\mathbf{x}$ .

101 The interaction equations between the fluid and the boundary are given by:

$$\mathbf{F}(\mathbf{x}, t) = \int \mathbf{f}(r, t) \delta(\mathbf{x} - \mathbf{X}(r, t)) dr \quad (3)$$

$$\mathbf{X}_t(r, t) = \mathbf{U}(\mathbf{X}(r, t)) = \int \mathbf{u}(\mathbf{x}, t) \delta(\mathbf{x} - \mathbf{X}(r, t)) d\mathbf{x} \quad (4)$$

102 where  $\mathbf{f}(r, t)$  is the force per unit length applied by the boundary to the fluid as a function of Lagrangian  
 103 position and time,  $\delta(\mathbf{x})$  is a two-dimensional delta function,  $\mathbf{X}(r, t)$  gives the Cartesian coordinates at  
 104 time  $t$  of the material point labeled by the Lagrangian parameter  $r$ . Equation 3 applies force from the  
 105 boundary to the fluid grid, and Equation 4 evaluates the local fluid velocity at the boundary. The boundary  
 106 is then moved at the local fluid velocity, and this enforces the no-slip boundary condition. Each of these  
 107 equations involves a two-dimensional Dirac delta function,  $\delta$ , which acts as the kernel of an integral  
 108 transformation. These equations convert Lagrangian variables to Eulerian variables and vice versa.

The force equations are specific to the application. In a simple case where a preferred motion is enforced, boundary points are tethered to target points via springs. The equation describing the force applied to the fluid by the boundary in Lagrangian coordinates is given by:

$$\mathbf{f}(r, t) = k_{targ} (\mathbf{Y}(r, t) - \mathbf{X}(r, t)) \quad (5)$$

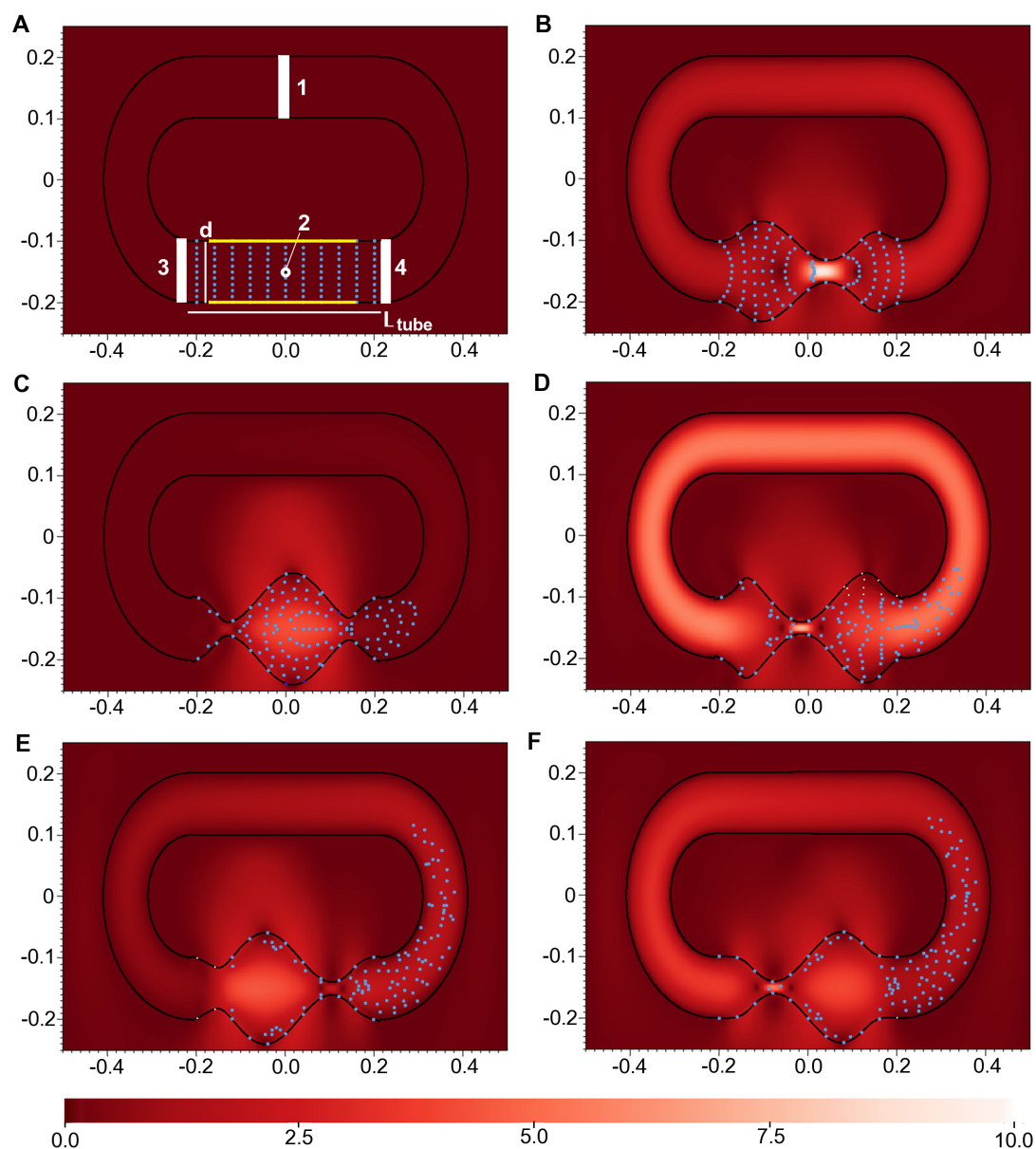
109 where  $\mathbf{f}(r, t)$  is the force per unit length,  $k_{targ}$  is a stiffness coefficient of the tethering springs, and  $\mathbf{Y}(r, t)$   
 110 is the prescribed position of the target boundary.

### 111 2.2 Dimensionless Numbers

To compare the flows of different pumps over a range of length scales and velocities, it is a useful exercise to non-dimensionalize the terms in the Navier–Stokes equations as follows,

$$\mathbf{x}' = \frac{\mathbf{x}}{L},$$

$$\mathbf{u}' = \frac{\mathbf{u}}{U},$$



**Figure 1.** Panels showing racetrack circulatory system and compression region with speed across the simulation area (background color) and light-blue flow marker particles. A: Initial simulation conditions ( $t = 0.0$ ) showing racetrack circulatory system (black lines), tube diameter  $d$  (white vertical line), compression region,  $L_{tube}$  (white horizontal line between white boxes 3 and 4), tethered region (yellow bars) and marker particles (light blue dots). Areas over which data were collected are labeled as white boxes and a white/black point (see text for details on calculations). B: Simulation at  $t = 0.4$ . C: Simulation at  $t = 0.8$ . D: Simulation at  $t = 1.2$ . E: Simulation at  $t = 1.6$ . F: Simulation at  $t = 2.0$ . Color scale units non-dimensional speed.

$$t' = f^* t,$$

112 where  $L$ ,  $U$ , and  $1/f^*$  are characteristic flow length, velocity, and time scales respectively. In this paper,  
 113 we choose  $L$  to be the diameter of the elastic section of the tube,  $f^*$  to be the beat frequency of our base  
 114 case, and the characteristic velocity as  $U = Lf^*$ . Note the  $U$  describes the velocity in terms of heart tube  
 115 lengths per beat.

The dimensionless bending stiffness of the boundary may then be calculated as

$$k'_{bend} = \frac{k_{bend}}{\rho U^2 L^3}, \quad (6)$$

where  $k_{bend}$  is the flexural stiffness of the boundary. The dimensionless spring stiffness may be written as

$$k' = \frac{k}{\rho U^2 L}, \quad (7)$$

116 where  $k$  is the spring stiffness which describes the resistance to stretching.

The dimensionless pressure can then be defined as

$$p' = \frac{p}{\rho U^2}, \quad (8)$$

117 where  $p$  is the dimensional pressure and  $U$  is the characteristic velocity.

Of particular relevance to internal biological flows is the Womersley number ( $Wo$ ). The  $Wo$  describes to what extent unsteady effects matter in pulsatile flows. It is given by the following equation,

$$Wo = d \sqrt{\frac{\omega}{\nu}}, \quad (9)$$

118 where  $\omega$  is the frequency of the pulse,  $d$  is the diameter of the tube, and  $\nu$  is the kinematic viscosity of the  
 119 fluid. Within the context of a blood vessel, when the value of  $Wo$  is high, the velocity profile is nearly  
 120 flat over most of the cross-section and there is a small region near the vessel wall known as the boundary  
 121 layer where viscous effects are important. Also, the flow at the center of the tube is inertial and pulsatile.  
 122 At the other low extreme end of  $Wo$ , the velocity profile over the vessel cross-section is parabolic, and the  
 123 flow is quasi-steady and viscous dominated. The transient effects can be ignored when  $Wo$  is sufficiently  
 124 small, generally when  $Wo < 1$ , and this is common in the case of microcirculation. Unless otherwise  
 125 noted, we vary the  $Wo$  by changing the viscosity of the fluid only.

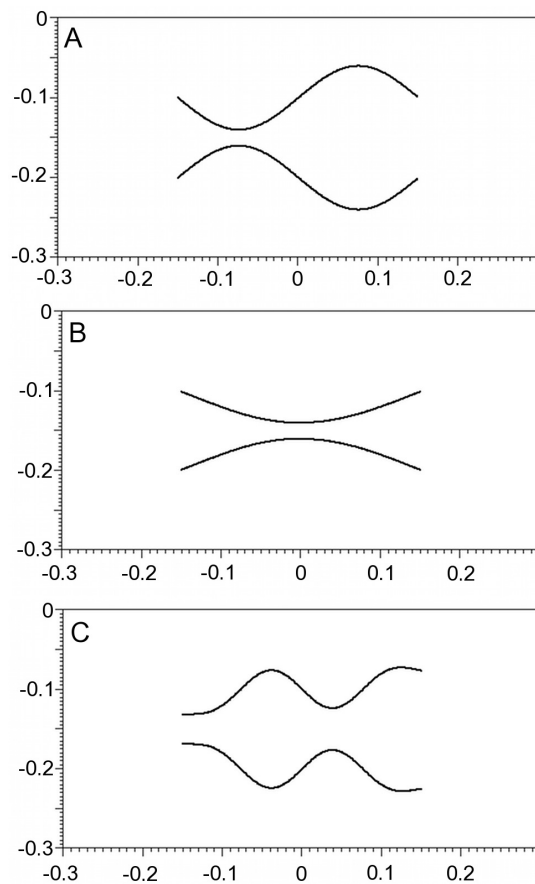
### 126 2.3 Numerical Method

127 We used an adaptive and parallelized version of the immersed boundary method, IBAMR (Griffith, 2014).  
 128 IBAMR is a C++ framework that provides discretization and solver infrastructure for partial differential  
 129 equations on block-structured locally refined Eulerian grids (Berger and Olinger, 1984; Berger and Colella,  
 130 1989) and on Lagrangian (structural) meshes. IBAMR also includes infrastructure for coupling Eulerian  
 131 and Lagrangian representations.

132 The Eulerian grid on which the Navier-Stokes equations were solved was locally refined near the  
 133 immersed boundaries and regions of vorticity with a threshold of  $|\omega| > 0.1$ . This Cartesian grid was  
 134 organized as a hierarchy of four nested grid levels, and the finest grid was assigned a spatial step size of  
 135  $dx = D/512$ , where  $D$  is the length of the domain. The ratio of the spatial step size on each grid relative  
 136 to the next coarsest grid was 1:4. The numerical parameters used for the simulations are given in Table 1.

### 137 2.4 Model of Peristalsis

138 A numerical model of an elastic heart tube connected to a rigid racetrack was constructed to study high  
 139 amplitude peristaltic flows. The racetrack design was used for easy comparison to previous models of  
 140 tubular heart pumping (e.g. Jung and Peskin, 2000; Hickerson et al, 2005b; Baird et al, 2014; Avrahami  
 141 and Gharib, 2008; Lee et al, 2012). The racetrack section was constructed by connecting two sections of  
 142 straight tube (one of which represents the elastic heart) to curved sections. The resting diameter of the  
 143 racetrack was constant throughout its length. Dimensions and elastic properties of the racetrack are given  
 144 in Table 2, and the model set up is shown in Fig. 1A.



**Figure 2.** Panels showing no-racetrack design and several waveforms at simulation time = 2 seconds. Waveforms are the result of keeping a constant speed of compression wave,  $c = 3.0$ , while altering the frequency of compression wave,  $f$ . A:  $f = 1.0$  (default value), B:  $f = 0.5$ , C:  $f = 2.0$ . Note that the domains in this figure have been reduce to show detail of the waveforms and do not reflect the domain on which the simulations were performed.

**Table 1.** Parameter values for two-dimensional immersed-boundary simulations.

Parameter	value
Maximum time step ( $dt$ )	0.00001
Minimum Eulerian spatial step ( $dx$ )	0.01952
Lagrangian spatial step ( $ds$ )	0.00976
Domain size ( $D$ )	10.0
Refinement ratio ( $R_f$ )	4:1

**Table 2.** Dimensionless parameter values for the peristalsis model.

Parameter	value
Length pumping section ( $L_{tube}$ )	4.0
Diameter ( $d$ )	1.0
Contraction frequency ( $f$ )	0.25 - 3
Womersley number ( $Wo$ )	0.1 - 50
Spring constant ( $k'$ )	0.03 - 100
Bending stiffness ( $k'_{bend}$ )	0.001 - 1
Wave speed ( $c$ )	1.67 - 6
y coordinate of top of tube ( $R_{top}$ )	-0.1
y coordinate of bottom of tube ( $R_{bot}$ )	-0.2
Amplitude of contraction ( $A$ )	$0.1d - 0.475d$
Compression ratio	0.40 - 0.95

The bottom portion of the racetrack consisted of an elastic section of dimensionless length  $L = 4.0$  and dimensionless diameter  $d = 1.0$ . The middle  $3/4$  of the tube was tethered to target points that drove the peristaltic motion. Note that the tube was initialized at rest in a straight configuration. The amplitude of the peristaltic wave increased from zero to its maximum amplitude after one pulse. To ensure conservation of volume inside the racetrack during pumping, the ends of the elastic section were allowed to deform as a result of the coupling between the elastic boundary and the fluid. Note that the sides and top of the racetrack were also tethered to target points that did not move. The target point stiffness,  $k_{targ}$  was set equal to the spring stiffness  $k$ . This parameter can be adjusted to minimize the distance between the actual boundary point and its target position. The position of the target points was determined by the following equation,

$$y_{top,bot} = R_{top,bot} \pm A \sin(2\pi ft + 2\pi cx_i) \quad (10)$$

where  $y_{top,bot}$  is the y-coordinate of the top or bottom of the tube,  $R_{top,bot}$  is the distance of the top or bottom of the tube from the horizontal centerline of the racetrack,  $A$  is the amplitude of the contraction,  $f$  is the frequency of contraction,  $c$  is the wave speed, and  $x_i$  is the horizontal distance from the beginning of the prescribed motion. The compression ratio gives the percent occlusion, and is equal to  $2A$ .

In addition to the racetrack design, we constructed an open model of peristalsis which consisted of only the elastic heart tube on the same domain (Fig. 2). The heart tube was driven in an identical way to the racetrack design. This design allowed us to eliminate the possibility of Liebau pumping in our closed, racetrack model by removing the flexible regions of heart tube that connected the contracting region to the rigid racetrack.

## 2.5 Parameter Sweeps

We varied the values of four parameters in five separate sets of simulations. 1)  $Wo$  was changed by altering the dynamic viscosity  $\mu$  of the fluid within the tube, which alters  $\nu$  in Equation 9 since  $\nu = \mu/\rho$ , where  $\rho$  is fluid density.  $Wo$  ranged from 0.1 to 10. 2) Tube occlusion was changed by altering the amplitude of contraction  $A$  in Equation 10 by some factor (compression ratio), which ranged from 40% tube occlusion (compression ratio = 0.4) to nearly complete occlusion of the tube (compression ratio = 0.95). 3) The speed of compression wave 4) the frequency of compressions ( $f$  in Equation 10) was changed, ranging from 0.5 to 2.0, while allowing the speed of compression wave,  $c$ , to increase linearly. 5) The frequency of compressions ( $f$  in Equation 10) was changed while holding the speed of the compression wave,  $c$ , constant. Note that the no-racetrack design was used only for sweeps of compression wave frequency.

The default parameter values used for simulation sweeps other than the parameter of interest are:  $Wo = 1$ ,  $f^* = 1$ ,  $c = 3.0$ , and compression ratio = 0.8.

## 2.6 Data Analysis

For each simulation, several calculations were made on fluid flow velocity in VisIt 2.5.2 (Childs et al, 2012) (for the racetrack design), Matlab (for the no-racetrack design), and R (Team, 2011) (both designs). The compression wave propagated along the compression tube from left to right which drove fluid flow in

170 the counter-clockwise direction around the racetrack (Fig. 1A-F). As a result, all positive flow speeds  
 171 indicate counter-clockwise flow (in the direction of the propagating compression wave) and negative  
 172 values indicate clockwise flow (opposite to the direction of the propagating compression wave).

173  $U_{avg}$ : At each time point in the simulation, the non-dimensional magnitude of velocity  $|\mathbf{u}'|$  of fluid  
 174 flow was spatially averaged across the cross-section of the upper tube of the racetrack indicated by a white  
 175 box labeled 1 in Fig. 1A. These mean speeds were then temporally averaged over the entire simulation to  
 176 find the average speed per simulation  $U_{avg}$ , presented in Fig. 5A-C (black circles) and Fig. 8A (black and  
 177 gray circles).

178  $U_{max,t}$ ,  $U_{max}$ : The non-dimensional maximum magnitude of velocity across the same section of  
 179 tube (white box labeled 1 in Fig. 1A) was also calculated for each time point of the simulation,  $U_{max,t}$ .  
 180 Fig. 3 shows  $U_{max,t}$  versus dimensionless time. These numbers were temporally averaged over the entire  
 181 simulation to find the average maximum speed per simulation,  $U_{max}$ , presented in Fig. 5A-C (white  
 182 diamonds) and Fig. 8A (white and gray diamonds).

183  $U_{peak}$ : Using the non-dimensional, maximum speeds across the upper section of tube (white box  
 184 labeled 1 in Fig. 1A) for each simulation time step, peak speeds (maximum of maximum speed) were  
 185 found for each pulse. For each simulation, the peak speeds over each pulse were averaged to find the  
 186 average peak speed for each simulation,  $U_{peak}$ .

187  $u_m$ ,  $u_{x,t}$ ,  $u_x$ : To characterize some of the dynamics in the compression region, the instantaneous,  
 188 non-dimensional magnitude of velocity ( $|\mathbf{u}'|$ , speed) and  $x$ -component of fluid flow velocity,  $u_{x,t}$ , were  
 189 sampled at each time at one point in the center of the compression tube, indicated by the white/black  
 190 dot labeled 2 in Fig. 1A. For the  $x$ -component of velocity, the instantaneous component of velocity for  
 191 each time step  $u_{x,t}$  versus  $t'$  are presented in Fig. 4. These speeds were then temporally averaged across  
 192 the entire simulation to find the average speed or magnitude of velocity ( $u_m$ ) and average  $x$ -component  
 193 of velocity ( $u_x$ ) for each simulation. These speeds are presented in Fig. 5D-F as black squares ( $u_m$ ) and  
 194 triangles ( $u_x$ ) and in Fig. 8B as black and gray squares ( $u_m$ ) and black and gray triangles ( $u_x$ ).

195  $p_{in}$ ,  $p_{out}$ ,  $\Delta p$ : Non-dimensional pressure,  $p'$ , at each time step in the simulation was spatially averaged  
 196 across two cross-sections of the racetrack near the compression region: the inflow region (Fig. 1A, white  
 197 box 3) and outflow region (Fig. 1A, white box 4). The inflow pressures were subtracted from the outflow  
 198 pressures to find the pressure difference at each time step and averaged across the entire simulation to find  
 199 the average inflow pressure  $p_{in}$ , the average outflow pressure  $p_{out}$ , and average pressure difference ( $\Delta p$ )  
 200 for each simulation. These pressures are presented in Fig. 7A-D as connected circles ( $p_{in}$ ), connected  
 201 diamonds ( $p_{out}$ ) and dotted triangles ( $\Delta p$ ).

202 For the no-racetrack design, the average volume flow rate  $v_{avg}$  was calculated using Matlab. The  
 203 average  $x$ -component of velocity across the opening of the heart tube was calculated and then divided  
 204 by the diameter of the opening at that time point. These values were then temporally averaged across  
 205 simulation time to find  $v_{avg}$ .

## 206 3 RESULTS

207 Results discussed below are for the racetrack design unless otherwise noted.

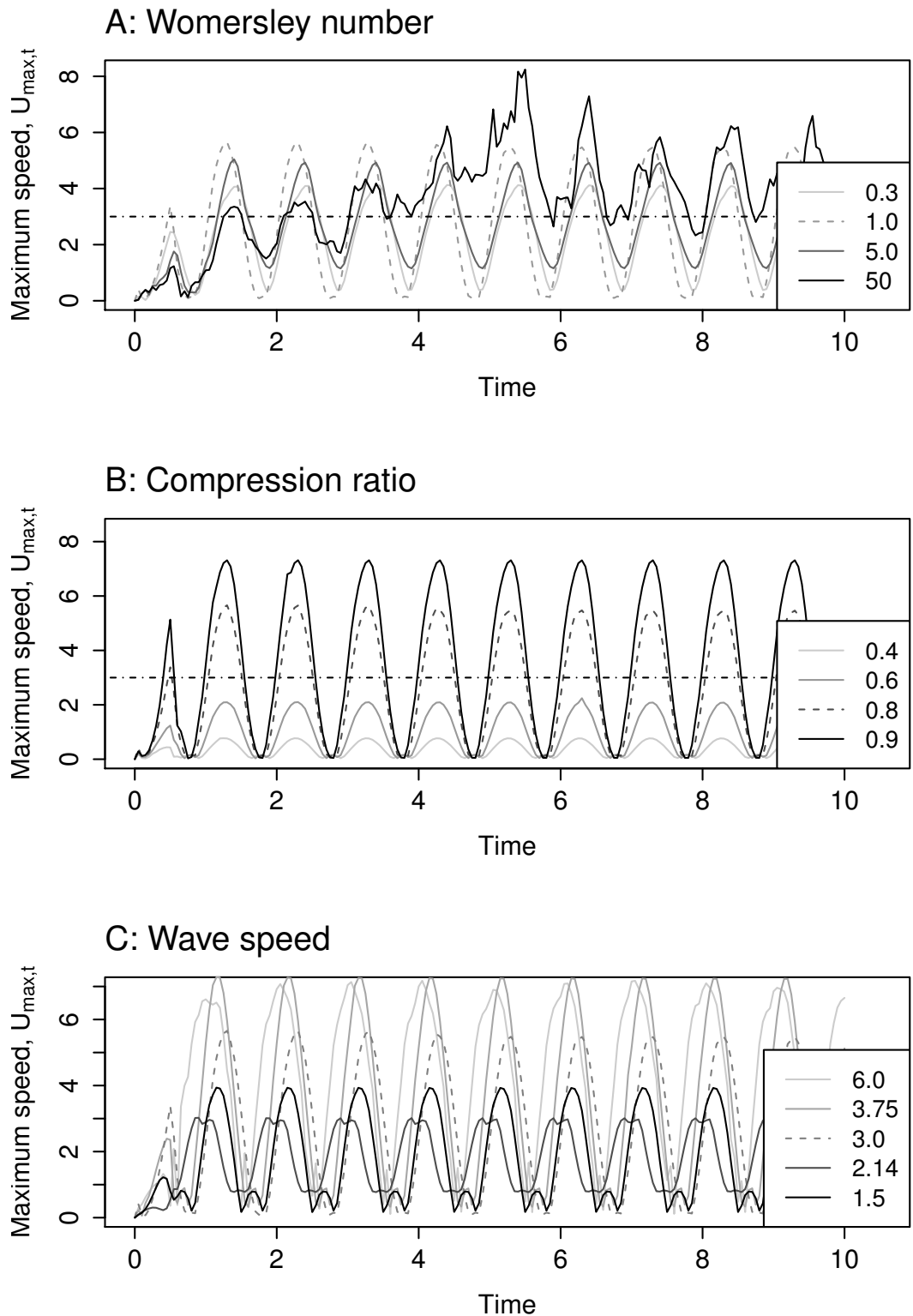
### 208 3.1 Womersley number

209 **Flow speeds in the racetrack.**  $U_{max,t}$  is graphed against simulation time for several  $Wo$  in Fig. 3A. Note  
 210 that the  $Wo$  was varied by changing the viscosity of the fluid rather than the pulse frequency and/or the  
 211 wave speed. The dashed line shows the constant wave speed for these simulations. Fluid flow speeds  
 212 exhibit pulsatile behavior for  $Wo$  of 5 and below. Unsteady behavior is observed for  $Wo = 50$ , likely due  
 213 to inertial effects and the formation of strong vortices in the tube. In all cases, the maximum dimensionless  
 214 flow speed is greater than the wave speed for part of the cycle.

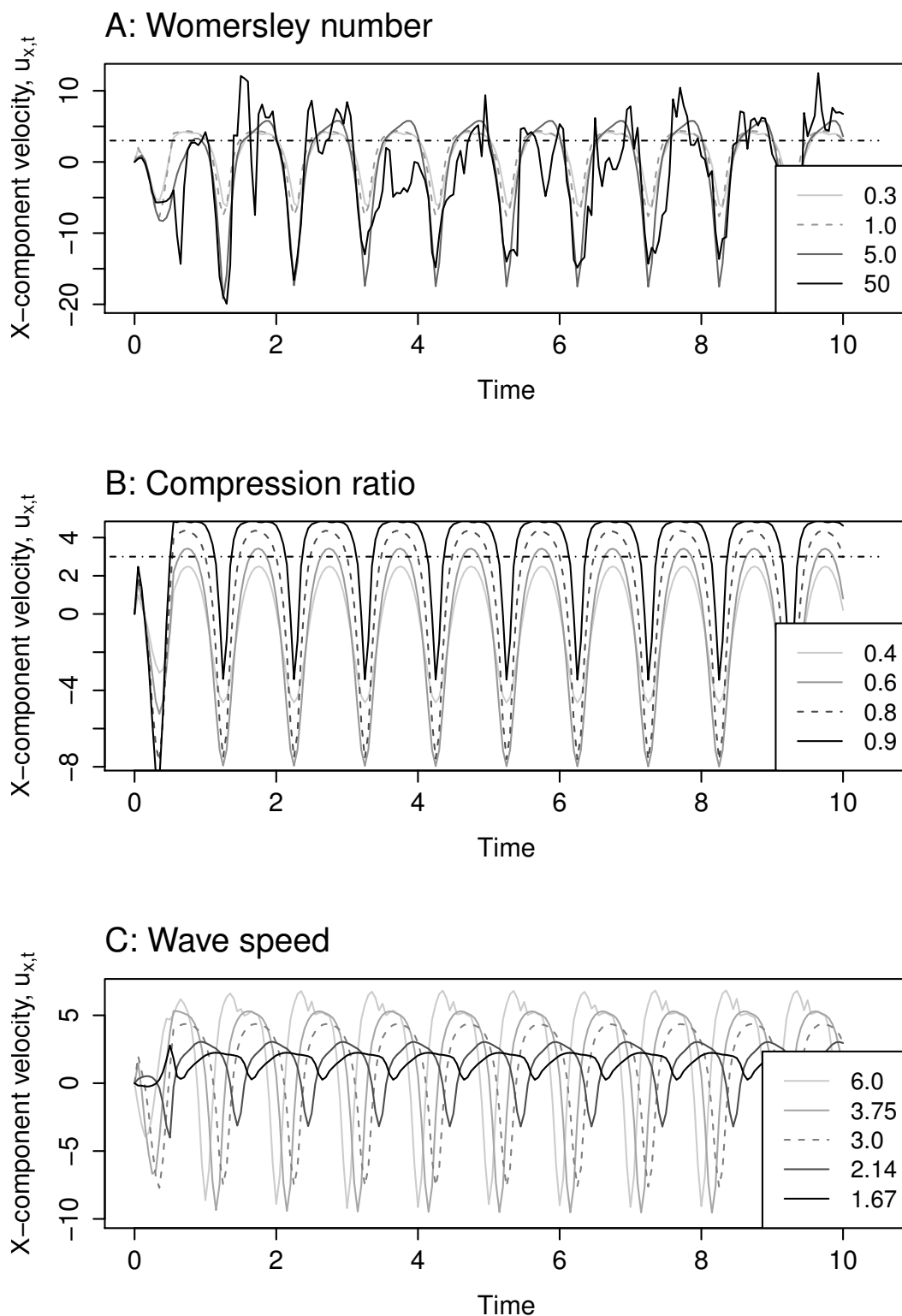
215  
 216  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  are graphed against Womersley number ( $Wo$ ) in Fig. 5A. Non-linear relation-  
 217 ships exist between each of the dimensionless flow speed metrics and  $Wo$ , where the  $Wo$  was varied by  
 218 changing the viscosity.  $U_{avg}$  tend to steadily increase with increasing  $Wo$ , while average peak flow speeds  
 219 are greatest around  $Wo = 1$  and 50.  $U_{peak}$  are greater than the speed of the compression wave,  $c$ , for all  
 220  $Wo$  and show variability with simulation time for values of  $Wo > 10$  (Fig. 3A).

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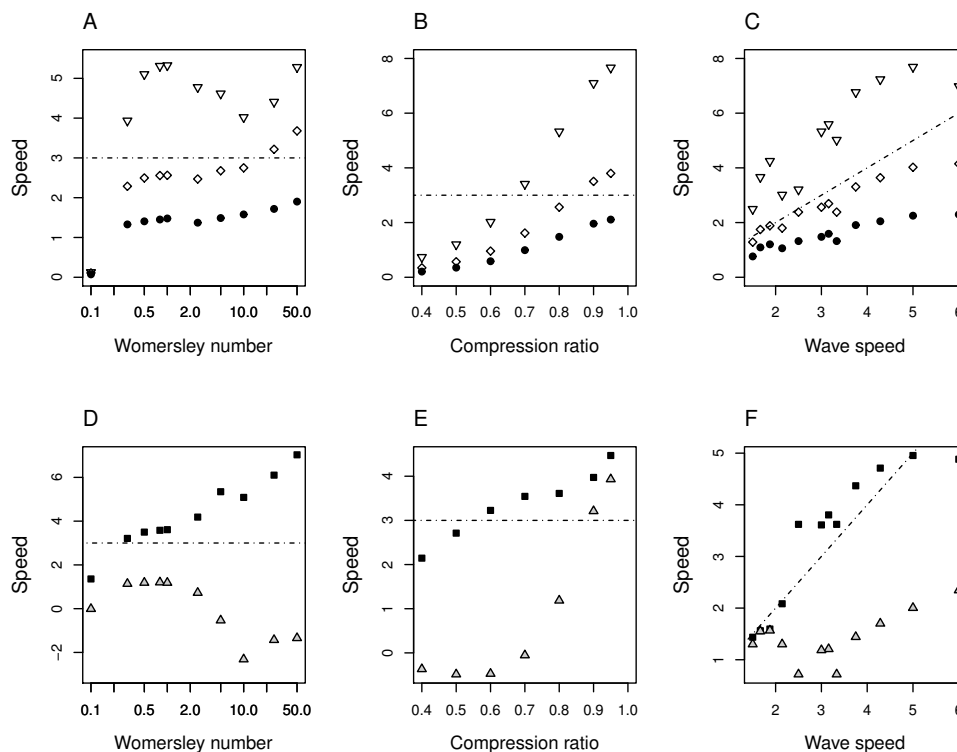




**Figure 3.**  $U_{max,t}$  vs. simulation time  $t'$ . Dotted lines indicate default values for each parameter. Positive speed indicates movement of fluid in the counter-clockwise direction around the racetrack. Horizontal dot-dash line indicates the non-dimensional speed of the compression wave for A and B. A: Womersley number, B: compression ratio, C: non-dimensional speed of the compression wave,  $c$ .



**Figure 4.**  $u_{x,t}$  vs. dimensionless time,  $t'$ , for a point at the center of the compression tube. Positive speed indicates movement of fluid in the counter-clockwise direction around the racetrack. Dotted lines indicate default values for each parameter. Horizontal dotted-dashed line indicates the non-dimensional speed of the compression wave,  $c$ , for A and B. A: Womersley number, B: compression ratio, C: non-dimensional compression wave speed,  $c$ .



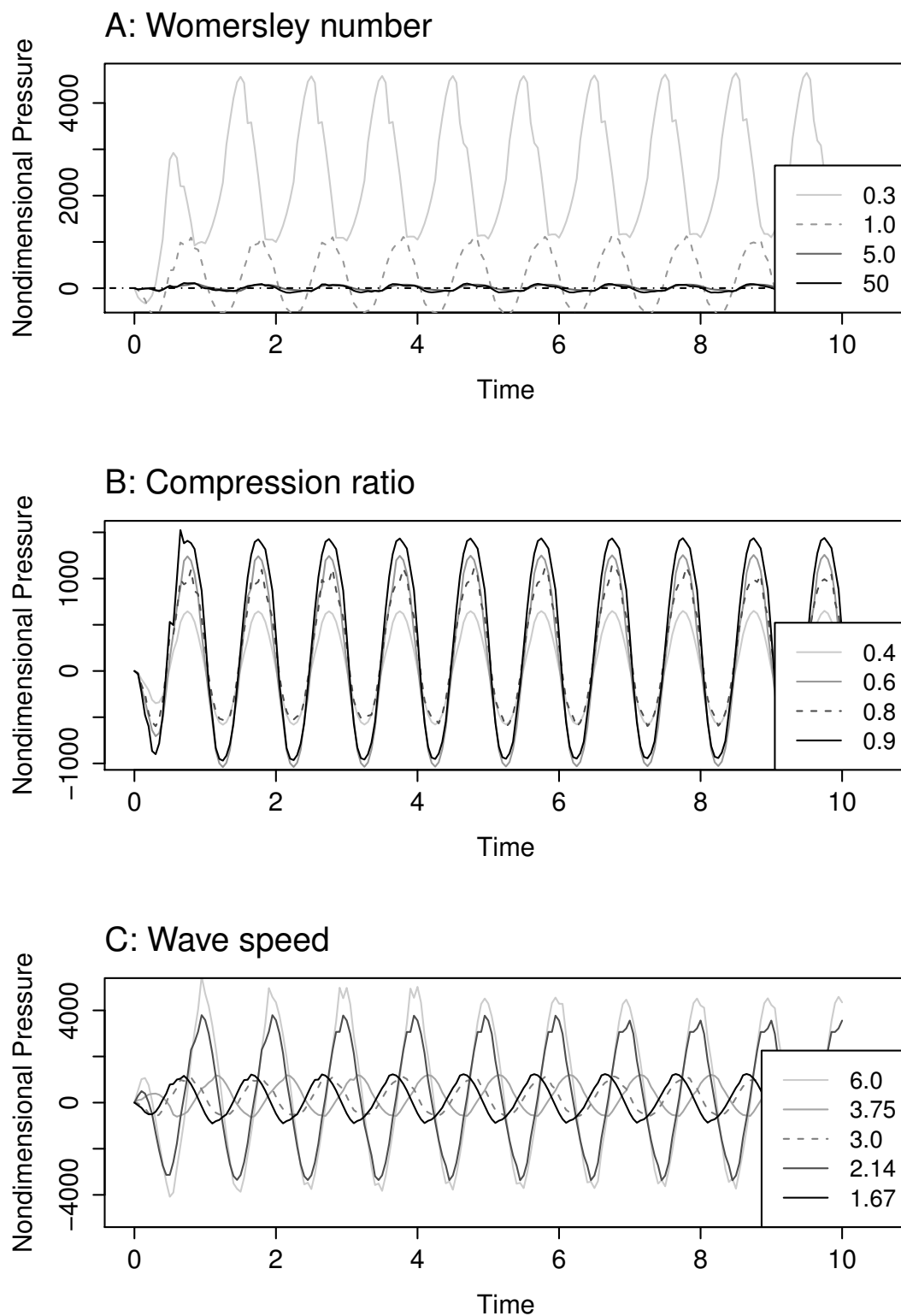
**Figure 5.** A-C: Non-dimensional fluid speeds within the racetrack versus parameter for  $U_{avg}$  (black circles),  $U_{max}$  (white diamonds), and  $U_{peak}$  (white, inverted triangles) across a section of tube (see text for details of calculations). Positive speed indicates movement of fluid in the counter-clockwise direction around the racetrack. D-F:  $u_m$  (black squares) and  $u_x$  (white triangles) vs. parameter for a point at the center of the compression tube. Non-dimensional compression wave speed,  $c$ , is noted on each plot as a dotted-dashed line. A,D: Womersley number, B,E: compression ratio, C,F: non-dimensional speed of the compression wave,  $c$ .

222 **Flow speeds within the compression tube.**  $u_m$  and  $u_x$  are plotted against  $Wo$  in Fig. 5D.  $u_{x,t}$  is plotted  
 223 against time for several simulations in Fig. 4A. The flow reversals (indicated by a change in sign) show  
 224 a non-parabolic flow profile in the pumping section for  $Wo \geq 10$ . While  $u_m$  at this point increases  
 225 with increasing  $Wo$ , the temporally averaged value of  $u_x$  decreases and becomes negative for  $Wo > 1$ .  
 226 This indicates that flow is moving on average in clockwise direction, or opposite the direction of the  
 227 propagating compression wave. This phenomenon is due to significant back flow that occurs when the  
 228 tube rapidly expands behind the compression wave.

229  
 230 **Pressure.** For values  $Wo < 2$ , there are large differences in pressure ( $\Delta p$ ). Since  $Wo$  is varied by changing  
 231 viscosity, the  $Wo < 1$  cases are viscous dominated, and this results in a high resistance of the fluid to  
 232 move through the tube.  $\Delta p$  are greatest at  $Wo = 0.3$ , with  $p' > 4000$  (Fig. 7A). Of note is the case where  
 233  $Wo = 0.1$  and the pressure difference decreases relative to  $Wo = 0.3$ . Note in Fig. 5A that the flow speed  
 234 at this  $Wo$  drops to almost zero. For a compression ratio of 0.8, the peristaltic pump is not able to drive  
 235 highly viscous flow around the racetrack, and the pressure difference between the inflow and outflow tracts  
 236 drops. For values  $W \geq 2$ , pressure differences between the two regions approach zero as the resistance to  
 237 flow decreases with decreasing viscosity. Non-dimensional pressure  $p'$  is reported versus time in Fig. 6A  
 238 for varying values of  $Wo$ .

### 239 3.2 Tube Occlusion

240 **Flow speeds in the racetrack.**  $U_{max,t}$  is graphed against dimensionless time for several compression  
 241 ratios in Fig. 3B. Note that  $U_{max,t}$  does not exceed  $c$  for compression ratios set to 0.6 and less. For



**Figure 6.**  $p'$  vs. dimensionless time,  $t'$ , for a point at the center of the compression tube. Dotted lines indicate default values for each parameter. Horizontal dotted-dashed line indicates the non-dimensional speed of the compression wave,  $c$ , for A and B. A: Womersley number, B: compression ratio, C: non-dimensional compression wave speed,  $c$ .

242 large compression ratios of 0.8-0.9,  $U_{max,t}$  reaches speeds of nearly double the value of  $c$ . In all cases  
243 considered,  $U_{max,t}$  is positive, and the flow moves in the counterclockwise direction at the top of the  
244 racetrack.

245  
246  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  are graphed against compression ratio in Fig. 5B. Each metric of the flow speed  
247 has a non-linear, increasing relationship with increasing compression ratios. For compression ratios  
248 under 0.7, corresponding to 70% tube occlusion,  $U_{peak}$  does not exceed  $c$  which is consistent with a  
249 low-amplitude approximation of peristalsis (Fig. 3B). However, for values 0.7 and above, the average  
250 peak flow speeds exceed  $c$ .

251  
252 **Flow speeds within the compression tube.** Fig. 4B reports  $u_{x,t}$  measured at the center of the com-  
253 pression region as a function of dimensionless time for different compression ratios. Note that in all  
254 cases, significant backflow occurs as the tube rapidly expands behind the compression wave. Backflow  
255 is minimized at the highest compression ratio of 0.9. Fig. 5E reports the temporally averaged speeds,  
256  $u_m$  and  $u_x$ , versus compression ratio. Higher compression ratios lead to higher forward flow speeds, as  
257 evidenced by the increase in  $u_x$  relative to overall magnitude in Fig. 5B.  $u_x$  exceeds the speed of the  
258 compression wave for the highest values ( $\geq 0.9$ ).  $u_m$  starts to exceed  $c$  as low as compression ratio = 0.6  
259 (Fig. 4B).

260  
261 **Pressure.** Pressure differences between the inflow region (Fig. 1A at 3) and outflow region (Fig. 1A at 4)  
262 are small for lower compression ratios and grow non-linearly with increasing tube occlusion (Fig. 7B).  
263 The higher pressure differences correspond to the larger flow speeds generated by the higher compression  
264 ratios. Non-dimensional pressure  $p'$  is reported versus time in Fig. 6B for varying values of compression  
265 ratio.

### 266 3.3 Speed of Compression Wave, $c$

267 **Flow speeds in the racetrack.** In this set of simulations, the pulsing frequency is held constant and  $c$   
268 is varied.  $U_{max,t}$  is graphed against dimensionless time for several wave speeds in Fig. 3C. Note that  
269 changing  $c$  while holding the frequency constant has the effect of changing the wave form (see Fig. 2).  
270 The base case wave speed,  $c = 3.0$  was halved and doubled. As expected, lower values of  $c$  resulted in  
271 slow flows and higher values of  $c$  resulted in faster flows.

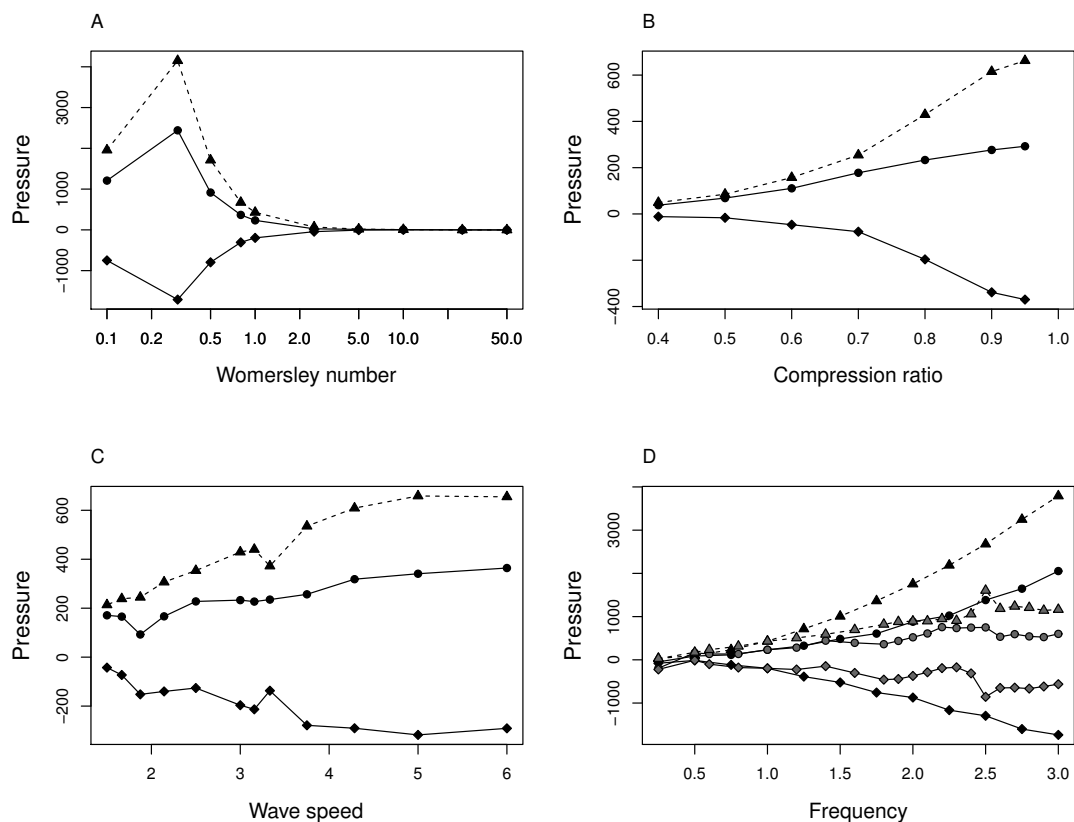
272  
273 Fig. 5C presents  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  versus  $c$  for the upper section of the racetrack. All three speeds  
274 have a non-linear and increasing relationship with increasing wave speed, with average peak speeds being  
275 consistently higher than  $c$ . There is a small dip in fluid speeds around value  $c = 3.33$  which is consistent  
276 across all three measures of fluid speed.

277  
278 **Flow speeds within the compression tube.** Fig. 4C reports  $u_{x,t}$  as a function of dimensionless time for  
279 different wave speeds. Note that there is significant backflow for the higher wave speed cases. In Fig. 5F,  
280 the temporally averaged speeds  $u_m$  and  $u_x$  measured at a point within the compression tube are plotted  
281 against the wave speed. All three speed metrics have a similar non-linear relationship with  $c$ . Speeds  
282 increase overall with increasing  $c$ .

283  
284 **Pressure.** Pressures across both the inflow region (Fig. 1A at 3) and outflow region (Fig. 1A at 4) shares  
285 a non-linear relationship with  $c$ , similar to the relationship seen between fluid flow speed and wave speed  
286 (Fig. 7C). Generally, increasing wave speed also increases the pressure difference between the two points.  
287 Note that the pressure difference dips around  $c = 3.33$ , just as  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  also drop at this  
288 value of  $c$ . Non-dimensional pressure  $p'$  is reported versus time in Fig. 6C for varying values of  $c$ .

### 289 3.4 Compression Wave Frequency

290 Here we consider the following two cases: 1) frequency and wave speed are varied proportionally such  
291 that the waveform along the compression tube is unchanged, and 2) frequency is varied while the wave  
292 speed is held constant. This allows us to consider the cases when wave speed is coupled to and decoupled  
293 from changes in the pulse frequency.



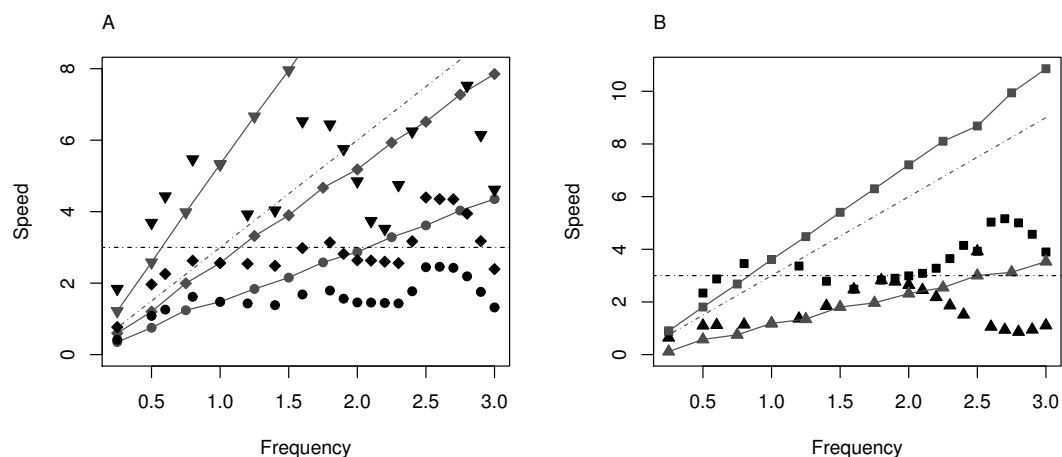
**Figure 7.** Pressure versus parameter across two sections of the racetrack.  $p_{in}$ : circles, solid line;  $p_{out}$ : black diamonds, solid line;  $\Delta p$ : black triangles, dotted line. A: Womersley number, B: compression ratio, C: non-dimensional speed of the compression wave,  $c$ , and D: non-dimensional compression-wave frequency,  $f$ . For D, frequencies with constant wave speed are gray and frequencies with varying wave speeds are black.

### 294 3.4.1 Variable Wave Speed

295 **Flow Speed.** Fig. 8A shows  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  as a function of the pulse frequency,  $f^*$ , for the  
 296 racetrack design. The grey data connected by lines shows the case when the compression wave speed is  
 297 allowed to change proportionally with  $f^*$ . In this case, all measures of speed show a linear relationships  
 298 with  $f^*$ . The dashed line shows the wave speed, and  $U_{max}$  is close to the wave speed across all frequencies  
 299 considered.  $U_{peak}$  also varies linearly with  $f^*$  and is higher than the wave speed. (Fig. 8B) shows  $u_m$   
 300 and  $u_x$  measured in the compression region as a function of  $f^*$ . The grey data shows the cases where  $c$   
 301 varies with  $f^*$ , and a clear linear relationship is observed. The linear relationships between flow speeds  
 302 ( $U_{avg}$  and  $U_{peak}$ ) and  $f$  for flows generated in the no-racetrack model as well (Fig 9A). Additionally,  $U_{peak}$   
 303 exceed  $c$  for the no-racetrack design.

305 **Volume Flow Rate.** For the no-racetrack design, the volume flow rate,  $v_{avg}$ , has a linear relationship with  
 306 compression frequency,  $f$ , when  $c$  increases with increasing  $f$  (Fig. 9C).

308 **Pressure.** Fig. 7D shows the relationship between pressure,  $p'$ , and compression frequency,  $f$ , for cases  
 309 when the wave speed,  $c$ , changes proportionally with frequency (black items).  $p'_{in}$  shows a nonlinear but  
 310 regular increase with increasing  $f$ , and  $p'_{out}$  shows a nonlinear decrease with increasing frequency. The  
 311 pressure difference,  $\Delta p$  between the inflow and outflow tract increases in a regular and nonlinear way  
 312 with  $f$ .



**Figure 8.** Non-dimensional fluid speed vs. non-dimensional compression wave frequency,  $f$ , for two cases: simulations with constant compression wave speed,  $c$ , (black items, no lines) or variable  $c$  (gray, solid line). Positive speed indicates movement of fluid in the counter-clockwise direction around the racetrack. A:  $U_{avg}$  (circles),  $U_{max}$  (diamonds), and  $U_{peak}$  (inverted triangles) measured in the upper tube of the racetrack. (See text for description of calculations.) B:  $u_m$  (squares) and  $u_x$  (triangles) measured at a point within the compression region of the tube.

### 313 3.4.2 Constant Wave Speed

314 **Flow speeds in the racetrack.** When compression wave speed is held constant while the pumping  
 315 frequency increases, all measures of fluid speed have markedly non-linear relationships with compression  
 316 frequency. Note that this has the effect of changing the wave form along the length of the compression  
 317 region. Within the upper section of the racetrack,  $U_{avg}$ ,  $U_{max}$ , and  $U_{peak}$  show an increasing, oscillatory  
 318 pattern with distinct peaks near  $f = 0.8, 1.6,$  and  $2.5$  (Fig. 8A). This pattern is more pronounced for  
 319 the  $U_{peak}$ .  $U_{peak}$  greatly exceed the compression wave speed,  $c$ .  $U_{peak}$  is triple the wave speed near  $f = 2.5$ .

320  
 321 **Flow speeds within the compression tube for the racetrack design.**  $u_m$  and  $u_x$  also share a non-linear  
 322 relationship with the contraction frequency,  $f$ . This graph is characterized by oscillations, but peak flow  
 323 speeds within the compression tube do not correspond to the pattern seen within the racetrack (Fig. 8B).

324  
 325 **Flow speeds for the no-racetrack design.**  $U_{avg}$  and  $U_{peak}$  show a similar non-linear relationship with  $f$   
 326 when  $c$  is held constant (the racetrack and no-racetrack designs are compared in Fig. 9B). Peaks in both  
 327 speeds are seen around  $f = 0.8, 1.6,$  and  $2.5$ . Values of  $U_{peak}$  are consistently above  $c$ .

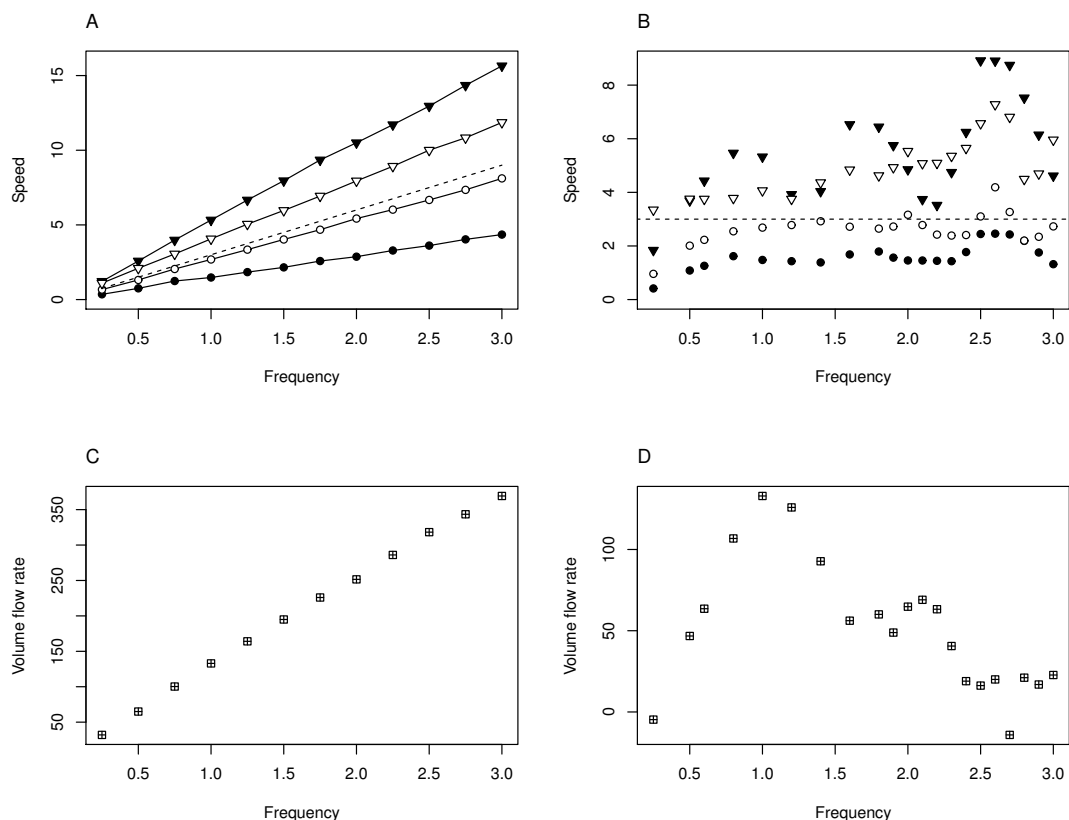
328  
 329 **Volume Flow Rate.** For the no-racetrack design, the volume flow rate,  $v_{avg}$ , has a non-linear relationship  
 330 with compression frequency,  $f$ , when  $c$  is held at 3.0 (Fig. 9D).

331  
 332 **Pressure.** Fig. 7D shows the relationship between pressures,  $p'_{in}, p'_{out}$  and  $\Delta p$ , and frequency,  $f$ , for  
 333 constant wave speed (gray items). Pressures show a non-linear relationship with frequency, as in the case  
 334 of fluid flow speed.

## 335 4 DISCUSSION

### 336 4.1 Evaluating large-amplitude, short-wave peristaltic pumps against the technical defi- 337 nition of peristalsis

338 Manner et al (2010) summarizes 6 qualities of technical peristaltic pumps often used to evaluate biological  
 339 pumps based on small-amplitude and/or long-wave approximation of peristalsis. Our direct, numerical  
 340 simulation of peristalsis adheres to a simpler, more inclusive definition of peristalsis: having a non-  
 341 stationary compression wave that travels uni-directionally down a tube with no structurally fixed direction



**Figure 9.** Top row: Non-dimensional fluid speed vs. non-dimensional compression wave frequency,  $f$ , for two cases: with a connected racetrack (black items) and with no circulatory system or rigid ends (white items). Positive speed indicates movement of fluid in the counter-clockwise direction around the racetrack.  $U_{avg}$  (circles) and  $U_{peak}$  (inverted triangles) measured in the upper tube of the racetrack (racetrack) and the mouth of the contracting region (no racetrack). Dotted lines report the speed of the compression wave,  $c$ . A. Simulations with variable  $c$ . B. Simulations with constant  $c$ . Bottom row: Volume flow rate,  $v_{avg}$ , versus compression-wave frequency,  $f$ , for C. simulations with with variable  $c$ , and D. simulations with constant  $c$ .

342 of flow. The geometry considered in this paper violates the long-wave approximation (the full wavelength  
 343 is 4 times the diameter for the base case) and the small-amplitude approximation (compressions up to  
 344 95% are considered). Furthermore, the  $Wo$  was varied from 0.1 to 50, spanning cases where both inertia  
 345 and viscosity are significant. Note that this model was not developed to capture the specific dynamics of  
 346 any particular tubular heart but rather to consider highly nonlinear dynamics.

347 Our models incorporates the most basic features of peristalsis and produces flow characteristics that  
 348 run counter to those listed in the technical definition. Our model generates pulsatile fluid flow for  $Wo$  of 5  
 349 and less at high compression ratios (Fig. 3A and B); flow speeds that show non-linear relationships when  
 350 either the compression wave speed or the pulsing frequency is fixed (Fig. 5C); and peak flow speeds that  
 351 exceed compression wave speeds in most cases (Figs. 3A-C, 5A-C, and 9A-B). These results are similar  
 352 to the results of other valveless, peristaltic models with cardiac cushions (Taber et al, 2007). When flow  
 353 speeds are measured in the compression section, significant back flow can be observed.

354 Additionally, the model shows that flow speeds can have either a linear or non-linear relationship  
 355 with compression frequency, depending on how the speed of the compression wave is handled. A linear  
 356 relationship between flow speed and compression frequency results when the speed of the compression  
 357 wave increases linearly with compression frequency (Figs. 8A and 9A,C), demonstrating that flow is  
 358 being driven by peristalsis and not another pumping mechanism. In this case, the wave form along the



359 tube is the same, and the pump just operates faster. This is a feature of most mechanical pumps that does  
360 not necessarily translate to biological pumps. In the case of a constant wave speed, the relationship is  
361 strikingly non-linear between fluid speed and compression frequency (Fig. 8A and 9B,D). For these cases,  
362 the wave form along the compression region changes (demonstrated in Fig. 2). This scenario corresponds  
363 to situations when the pacemaker activity is altered while the propagation speed of an action potential is  
364 constant.

#### 365 **4.2 Implications of large-amplitude, short-wave peristaltic pumps in biological fluid trans-** 366 **port systems**

367 Since many of the principles of the technical definition derived from mechanical pumps are violated by  
368 our simple model, we suggest that the technical definition of peristalsis is inappropriate for evaluating the  
369 pumping mechanism of biological pumps. While the definition appropriately describes some peristaltic  
370 pumps, many biological pumps may fail simply because they violate the low-amplitude, long-wave  
371 approximation used to establish the criteria in the technical definition. Simply decoupling compression  
372 wave speed and frequency can also cause a pump to violate the technical definition even though it retains  
373 the essential features of peristalsis (traveling wave of compression and no structurally fixed flow direction)  
374 that mathematicians and biologists use.

375 There are many biological pumps that fail criteria in the technical definition of peristalsis but fit the  
376 more inclusive definition. In tunicate hearts, heart beat frequency increases with increasing ambient  
377 temperature but the conduction velocity that passes down the heart tube remains constant (Kriebal, 1967).  
378 In mosquito hearts, hemolymph flow is not continuous and flow speed is greater than compression wave  
379 speed (Glenn et al, 2010). For many tubular pumps, the contraction wave may nearly or even completely  
380 occlude the tube. Other tubular pumps, such as the embryonic hearts of tunicates, are not much longer  
381 than they are wide. Tubes with diameters on the order of their length violate the long-wave assumption.

#### 382 **4.3 Significance of the pumping mechanism to the embryonic heart**

383 In the past 8 years, both peristalsis and dynamic suction pumping have been proposed as the mechanism  
384 by which the early embryonic heart tube drives the flow of blood. The important point of this difference  
385 for the case of understanding the evolution and development of the heart is the distinction between which  
386 regions of the heart actively contract. If tubular hearts pump using dynamic suction pumping, then only  
387 one region of the heart actively contracts, and the waves observed are passive and elastic. On the other  
388 hand, if the pumping mechanism is peristalsis, then the heart actively contracts along its entire length.  
389 This distinction has consequences for how the cardiac conduction system and the musculature develops.

390 In Forouhar et al (2006), work on embryonic zebrafish hearts, they present observations that demon-  
391 strate this valveless, tubular heart violates the technical definition of peristalsis. As we've shown with  
392 this simple model of flow being driven by peristalsis, fluid flow can mimic each observation made on the  
393 embryonic heart, including pulsatile flow both within the compressing tube (Fig. 4A-C) and far away from  
394 the compression tube (Fig. 3A-C); peak flow speeds that exceed compression wave speeds (Fig. 5A-F and  
395 9A-B); and a non-linear relationship between fluid flow and compression frequency that is very similar to  
396 the relationship observed in their study (Fig. 8A and 9B). The results of our study suggest that peristalsis  
397 cannot be ruled out as the pumping mechanism of the vertebrate embryonic heart, and that the exact  
398 pumping mechanism requires further study since both mechanisms can result in similar features for cases  
399 with nearly complete occlusion and diameter to length ratios on the order of 1:4.

400 The only observation that supports rejection of peristalsis as the pumping mechanism for the zebrafish  
401 heart is that no active contraction down the length of tube was observed (Forouhar et al, 2006). However,  
402 this observation has been disputed by others (Männer et al, 2010; Maes et al, 2011; Goenezen et al, 2012)  
403 and was not supported by direct measurement of muscle activation or morphological features that would  
404 suggest electrical activation of cardiac muscle was limited to one area of the heart. Many studies show  
405 that the architecture required to propagate such a signal are present early during heart development and  
406 that conduction throughout the myocardium is itself a critical component of normal cardiogenesis (Paff,  
407 1938; Paff et al, 1964; Rottbauer et al, 2001; Chi et al, 2010).

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