

On the quantification and visualization of transient periodic instabilities in pulsatile flows

*Original*

On the quantification and visualization of transient periodic instabilities in pulsatile flows / Khan, M.O., Chnafa, C., Gallo, D., Molinari, F., Morbiducci, U., Steinman, D.A., Valen Sendstad, K.. - In: JOURNAL OF BIOMECHANICS. - ISSN 0021-9290. - 57:(2017), pp. 179-182. [10.1016/j.jbiomech.2016.12.037]

*Availability:*

This version is available at: 11583/2662908 since: 2018-02-20T12:06:12Z

*Publisher:*

Elsevier Ltd

*Published*

DOI:10.1016/j.jbiomech.2016.12.037

*Terms of use:*

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

*Publisher copyright*

(Article begins on next page)

## Author's Accepted Manuscript

On the Quantification and Visualization of  
Transient Periodic Instabilities in Pulsatile Flows

Muhammad Owais Khan, Christophe Chnafa,  
Diego Gallo, Filippo Molinari, Umberto  
Morbiducci, David A. Steinman, Kristian Valen-  
Sendstad



PII: S0021-9290(16)31330-6  
DOI: <http://dx.doi.org/10.1016/j.jbiomech.2016.12.037>  
Reference: BM8070

To appear in: *Journal of Biomechanics*  
Accepted date: 21 December 2016

Cite this article as: Muhammad Owais Khan, Christophe Chnafa, Diego Gallo, Filippo Molinari, Umberto Morbiducci, David A. Steinman and Kristian Valen-Sendstad, On the Quantification and Visualization of Transient Periodic Instabilities in Pulsatile Flows, *Journal of Biomechanics* <http://dx.doi.org/10.1016/j.jbiomech.2016.12.037>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and a review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

# On the Quantification and Visualization of Transient Periodic Instabilities in Pulsatile Flows

Muhammad Owais Khan<sup>a,d,\*</sup>, Christophe Chnafa<sup>a</sup>, Diego Gallo<sup>b</sup>, Filippo Molinari<sup>c</sup>, Umberto Morbiducci<sup>b</sup>,  
David A. Steinman<sup>a</sup>, Kristian Valen-Sendstad<sup>d</sup>

<sup>a</sup>Department of Mechanical and Industrial Engineering, University of Toronto, Toronto, ON, Canada

<sup>b</sup>Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Torino, Italy

<sup>c</sup>Department of Electronics and Telecommunications, Politecnico di Torino, Torino, Italy

<sup>d</sup>Computational Cardiac Modeling Department, Simula Research Laboratory, Lysaker, Norway

## Abstract

*Turbulent-like flows without cycle-to-cycle variations are more frequently being reported in studies of cardiovascular flows. The associated stimuli might be of mechanobiological relevance, but how to quantify them objectively is not obvious. Classical Reynolds decomposition, where the flow is separated into mean and fluctuating velocity components, is not applicable as the phase-average is zero. We therefore expanded on established techniques and present the idea, analogous to Reynolds decomposition, to decompose a flow with transient instabilities into low- versus high frequency components, respectively, to discriminate flow instabilities from the underlying cardiac pulsatility. Transient wall shear stress and velocity signals derived from computational fluid dynamic simulations were transferred to the frequency domain. A high-pass filter was applied to subtract the 99% most-energy-containing frequencies, which gave a cut-off frequency of 25Hz. We introduce here the spectral power index, and compute the fluctuating kinetic energy, based on the high-pass filtered velocity components, both being frequency-based operators. The efficacy was evaluated in an aneurysm model for multiple flow rates demonstrating transition to turbulent-like flows. The frequency-based operators were found to better correlate with the qualitatively observed flow instabilities compared to conventional descriptors, like time-averaged wall shear stress or oscillatory shear index. We demonstrate how the high frequencies beyond the physiological range could be analyzed and/or transferred back to the time domain for quantification and visualization purposes. We have introduced general frequency-based operators, easily extendable to other cardiovascular territories based on a posteriori heuristic filtering that allows for separation, isolation, and quantification of cycle-invariant turbulent-like flows.*

**Keywords:** Hemodynamics, Cycle-Invariant Turbulent-Like Flows, Visualization, Spectral Power Index, Fluctuating Kinetic Energy

## 1. Introduction

Hemodynamic forces, particularly wall shear stress (WSS), are thought to contribute to vessel wall adaption and remodeling (Malek et al., 1999; Morbiducci et al., 2016). Since direct measurements of these stresses are difficult, medical image-based computational fluid dynamics (CFD) (Taylor and Steinman, 2010)

\*For correspondence: Kristian Valen-Sendstad, Simula Research Laboratory, Lysaker, Norway. Email: kvs@simula.no

16 has been extensively used in the investigation of vascular pathology. Except for aortic flows with Reynolds  
17 numbers ( $Re$ ) in the thousands (Nerem et al., 1972), cardiovascular flows have conventionally been considered  
18 laminar and stable; however, recent advances in imaging tools, as well as focus on numerical accuracy have  
19 highlighted the presence of transitional and turbulent-like flows (Valen-Sendstad et al., 2011; Chnafa et al.,  
20 2014; Valen-Sendstad et al., 2014; Zajac et al., 2015), consistent with experimental evidence (Roach et al.,  
21 1972; Yagi et al., 2013) and clinical observations (Ferguson, 1970; Kurokawa et al., 1994). The arterial  
22 stimuli from such turbulent-like flows have been linked, both *in vivo* (Fry, 1968) and *in vitro* (Davies et al.,  
23 1986), to adverse vascular remodeling. However, there appears to be no consensus in the literature on how  
24 to robustly quantify such turbulent-like flows.

25 While methods for decomposing the mean and transient parts of truly turbulent flows are well under-  
26 stood (Pope, 2000), for pulsatile flows this can only be applied in a phase-averaged sense, for flows with  
27 instabilities that vary from cycle to cycle (Chnafa et al., 2014; Poelma et al., 2015). Proper orthogonal  
28 decomposition (Grinberg et al., 2009) is an alternative method that allows for distinction between flow  
29 phenotypes and higher fluctuating components in cycle-invariant flows. However, the mechanobiological rel-  
30 evance of hemodynamic stresses reconstructed from high-mode velocity fields requires further investigation.  
31 Instead, initial ad hoc attempts in the biomedical literature have been focused on analyzes or visualizations  
32 of 1D velocity-time traces from selected points (Valen-Sendstad et al., 2013; Bozzetto et al., 2015; Varble  
33 et al., 2016). However, these traces are subjectively placed, provide a limited amount of information, and  
34 do not allow for additional post-processing or make complete use of the available 3D flow field.

35 Conventional hemodynamic WSS-based descriptors like time-averaged WSS and Oscillatory Shear Index  
36 (OSI) were originally developed for unsteady laminar flow regimes, and thus are not necessarily adequate  
37 descriptors of turbulent-like flow stimuli. The aim of the current study was to investigate a robust approach  
38 to quantify and visualize these turbulent-like flows. We propose frequency-based operators, which, analogous  
39 to Reynolds decomposition, decompose a signal into low- and high-frequency components. We demonstrate  
40 how this method can be applied to detect, characterize, quantify, and visualize high-frequency instabilities  
41 of volumetric and surface quantities, focusing on a cerebral aneurysm as a representative example.

## 42 2. Methods

43 We took advantage of methods frequently used, e.g., in turbulence research (Pope, 2000), where any  
44 signal can be transferred from the time domain to the frequency domain. Taking this approach, any heuristic  
45 filter can be applied to analyze the low versus high frequency components, and (potentially) transfer the  
46 harmonics back to the time domain for additional analyses and visualization purposes. Analogous to Reynolds  
47 decomposition, the signal reconstructed from low- versus high-frequencies are comparable to the phase-  
48 average versus fluctuating components, respectively.

49 Figure 1 illustrates this principle where the 1D time-velocity trace in red was decomposed using a high  
50 pass filter. The low frequency physiological 'carrier' signal is shown in black, while the high frequency

51 residual is shown in blue, reflecting the 'unphysiological' fluctuating components. We emphasize that this  
 52 applies to any 1D signal, like velocity, pressure, or WSS trace, but can also be assembled to surface and  
 53 volumetric quantities, respectively.

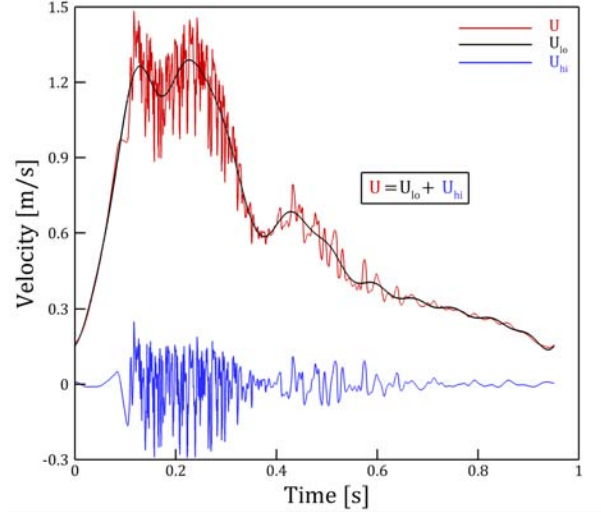


Figure 1: Visual representation of a cycle-invariant unstable flow and the of subtraction of the 99% most energy-containing-frequencies. The inset equation shows the analogy to Reynolds decomposition where  $U_{lo}$  is equivalent of the phase-average while  $U_{hi}$  is equivalent of the fluctuating component.

Inspired by the harmonic index defined as the fraction of harmonic amplitude spectrum arising from pulsatile flow component (Gelfand et al., 2006), we defined the spectral power index (SPI):

$$\text{SPI} = \frac{\sum_{n=n_c}^{+\infty} |Y[n\omega_0]|^2}{\sum_{n=1}^{+\infty} |Y[n\omega_0]|^2} \quad (1)$$

54 Where  $|Y[n\omega_0]|$  is the magnitude of the Fourier-transformed signal,  $\omega_0$  is the fundamental angular fre-  
 55 quency of the periodic signal,  $n_c$  is the harmonic corresponding to the cut-off frequency. To objectively  
 56 determine  $n_c$  in order to exclude frequencies in the normal physiological range, we subtracted harmonics  
 57 that contained 99% of the energy in the driving flow rate waveform, which resulted in a cut-off frequency  
 58 of  $n_c=25\text{Hz}$ . We emphasize two key differences from the harmonic index by Gelfand et al. (Gelfand et al.,  
 59 2006): i) SPI does not include the pulsatile waveform mean in the denominator, such that summation begins  
 60 from the first harmonic, ii) SPI is based on the power of the signal instead of the energy, to better highlight  
 61 energy content at higher frequencies. SPI is, therefore, a normalised quantity having the desirable property  
 62 of being on the interval  $[0 - 1]$ ; zero meaning that there are no flow instabilities while the scalar value 1  
 63 would reflect a completely unstable flow. Analogous to turbulence kinetic energy (TKE), we also computed  
 64 the time-averaged fluctuating kinetic energy (FKE), defined as:

$$\text{FKE} = \frac{1}{2}(\overline{u_{hi}^2} + \overline{v_{hi}^2} + \overline{w_{hi}^2}) \quad (2)$$

65 In contrast to Varble et al. (2016) who used a steady inflow, we here applied eq. (2) to a pulsatile  
 66 waveform where  $u_{hi}$ ,  $v_{hi}$  and  $w_{hi}$  are the high-pass filtered velocity components and the overline refers to the  
 67 time average. To evaluate the efficacy of frequency based operators, we chose an aneurysm model from the  
 68 open-source Aneurisk database (Aneurisk-Team, 2012). We specified a fully developed Womersley velocity  
 69 profile at the inlet, with a cross sectional mean velocity of  $.27\text{ m/s}$  (Valen-Sendstad et al., 2015) giving a base  
 70 flow rate of  $Q = 5.37\text{mL/s}$  with a period of  $0.951\text{s}$ . The flow rate was also reduced to  $.75Q$ ,  $.5Q$ , and  $.25Q$  to  
 71 demonstrate the onset of flow instabilities. The Vascular Modelling ToolKit (Antiga et al., 2008) was used  
 72 to generate a mesh with four boundary layers that consisted of three million tetrahedron cells, equivalent in  
 73 spatial resolution to the 'Medium' (HR5) simulations in (Khan et al., 2015), previously demonstrated to be  
 74 sufficient to resolve WSS and OSI.

75 Pulsatile CFD simulations were performed using the CFD solver *Oasis*, taking 10,000 time steps per cycle.  
 76 *Oasis* uses a projection scheme where special care has been taken to maintain a second-order accuracy  
 77 in space and time (Simo and Armero, 1994) to obtain a solution that preserves kinetic energy while mini-  
 78 mizes numerical dispersion and diffusion errors. For details regarding the implementation and order-optimal  
 79 convergence results, we refer to (Mortensen and Valen-Sendstad, 2015). Post-processing was based on 2500  
 80 time steps, corresponding to Nyquist limit of  $1314\text{Hz}$ . SPI applied to WSS-time traces ( $SPI_{WSS}$ ) and FKE  
 81 were then compared against nominal descriptors like the WSS normalised to the parent artery (TAWSS)  
 82 and OSI.

### 83 3. Results

84 Figure 2 (a) shows the chosen model and velocity magnitude traces in the carotid siphon, middle cerebral  
 85 artery and the aneurysmal sac for  $0.25Q$ ,  $0.5Q$ ,  $0.75Q$  and  $Q$ . While traces for  $0.25Q$  and  $0.5Q$  do not  
 86 feature evident high-frequency fluctuations, the complexity of the traces for  $0.75Q$  and  $Q$  are indicative of a  
 87 turbulent-like flow, especially in the aneurysm sac.

88 From the corresponding qualitative maps shown in Figure 2 (b), we note only a modest increase in the  
 89 parent artery normalised TAWSS maps with increasing flow rates. Regions of elevated OSI were found  
 90 for relatively stable flows  $0.25Q$  and  $0.5Q$ , but also for turbulent-like flows,  $0.75Q$  and  $Q$ . This is reflected  
 91 through the inset traces showing the WSS magnitudes recorded at a location on the sac dome marked with  
 92 a circle. In short, locations of high OSI are relatively unaffected by flow rate; what is affected is their extent,  
 93 but approximately linearly with flow rate. Broadly, these maps indicate that both TAWSS and OSI are  
 94 unable to discriminate laminar from turbulent-like flow stimuli.

95 On the other hand, a distinct increase in  $SPI_{WSS}$  was observed between  $0.5Q$  and  $0.75Q$ , consistent  
 96 with the appearance of higher-frequencies observed in filtered WSS time-magnitude traces, cf., inset figure.  
 97 Evident from these plots is that  $SPI_{WSS}$  is sensitive to flow destabilization and is able to discriminate  
 98 between stable and unstable stimuli. Similar trends were observed for cycle-averaged volumetric FKE maps;

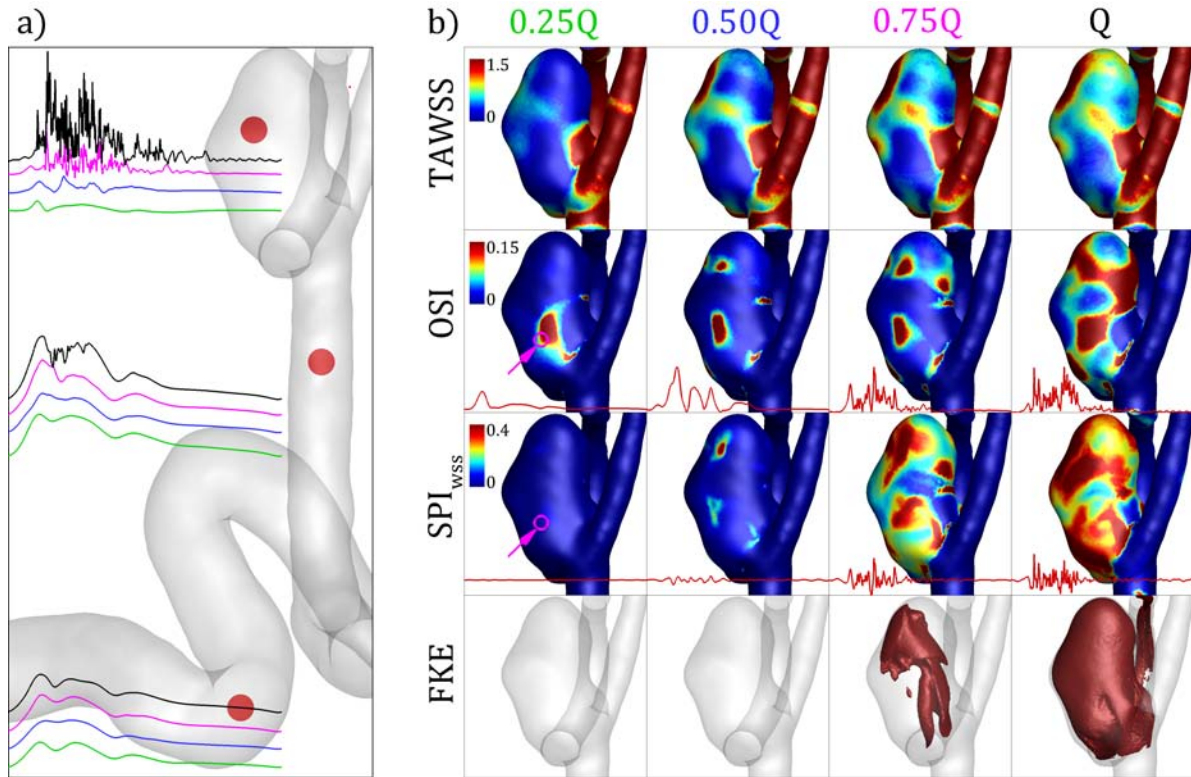


Figure 2: A) Chosen model and velocity traces at various locations normalised by the cycle mean. B) The hemodynamic indices TAWSS, OSI,  $SPI_{WSS}$ , and FKE for increasing flow rates.

99 no FKE is observed for 0.25Q and 0.50Q. However, distinct regions of FKE were observed for 0.75Q and Q,  
 100 correlating with the presence of high-frequency instabilities in the flow.

101 Focusing now on quantitative results shown in Table 1, we note that while sac-averaged values of TAWSS  
 102 and OSI increase approximately linearly as a function of flow rate,  $SPI_{WSS}$  and FKE show a sharp increase  
 103 between 0.50Q and 0.75Q, correlating with the appearance of high-frequency flow fluctuations. Being primarily  
 104 interested in the differences between 0.50Q and 0.75Q, we observe that  $SPI_{WSS}$  showed a 6-fold increase from  
 105 0.50Q to 0.75Q whereas TAWSS and OSI only increased by 20% and 70%, respectively.

106 Finally, as shown in the online supplementary material, animation of the high-pass filtered reconstructed  
 107 velocity field better highlights the flow instabilities due to a narrower dynamic range, compared to an  
 108 animation of the complete velocity field.

#### 109 4. Discussion

110 Although all of the building blocks are well-known, we have described here general frequency-based  
 111 operators for filtering, visualization, and analysis of turbulent-like flow features that can be assembled on  
 112 surfaces and volumes. The concept is readily extendable to cycle-invariant turbulent-like flows of other  
 113 cardiovascular territories, allowing for objective separation, isolation, and quantification of flow instabilities.

Table 1: Sac surface- or volume-averaged indices quantifying the marked increase for  $SPI_{WSS}$  and FKE, whereas TAWSS and OSI increase linearly with flow rates and/or time-averaged parent artery Reynolds number.

Flow rate	0.25Q	0.5Q	0.75Q	Q
Re [-]	97.5	195	292.5	390
TAWSS [-]	0.46	0.71	0.86	0.91
OSI [-]	0.013	0.024	0.041	0.096
$SPI_{WSS}$ [-]	0.004	0.037	0.220	0.325
FKE [ $m^2/s^2$ ]	0	0	0.003	0.011

114 In addition, this method can also be used for flows harbouring cycle-to-cycle fluctuations to separate inter-  
115 cycle and intra-cycle variations.

116 OSI is frequently argued to be a metric of 'disturbed flow', and has been demonstrated to be effective (Ku  
117 et al., 1985) even if incomplete descriptor (Gallo et al., 2016). However, it cannot discriminate slow, unidirec-  
118 tional oscillatory flow from fast, multidirectional variations, as shown in Figure 2 and discussed in previous  
119 studies (Peiffer et al., 2013; Valen-Sendstad and Steinman, 2014; Khan et al., 2015). As mentioned in the  
120 introduction, turbulent-like flows have been linked both *in vitro* and *in vivo* to adverse vascular remodel-  
121 ing. As an example, we previously reported an "intriguing albeit incidental" correlation between TKE and  
122 aneurysm rupture status (Valen-Sendstad et al., 2013), under steady state inflow. SPI is an example of a  
123 metric that is reduced to a single number allowing for mapping of hotspots of turbulent WSS under more  
124 realistic pulsatile flows. SPI could also be integrated volumetrically (e.g., over the aneurysm sac) as a single  
125 objective marker of unstable flow phenotype. Rank-ordering turbulent-like flows based on SPI is indeed  
126 possible. That being said, we have only demonstrated this in a single aneurysm case. Furthermore, one  
127 limitation is that while SPI is a good descriptor of the most 'active' regions of the WSS, using our exact  
128 definition one cannot distinguish between various frequencies. Namely, it cannot discriminate low broad-  
129 band fluctuations from a high narrowband 'spike', nor does it provide information about which frequencies  
130 are dominant. One could, however, decompose SPI into frequency bands, which could be used to highlight  
131 instabilities at different frequency ranges. By definition, if those bands are contiguous, those individual SPI  
132 would add up to the total SPI. Finally, the cut-off frequency described in the methods was adopted because  
133 it can be applied objectively to any driving flow waveform, although future biological investigations may  
134 uncover specific frequency bands of interest, and in a broader sample of vascular applications.

## 135 5. Conclusion

136 We have described general frequency-based operators that are easily extendable to other cardiovascular  
137 territories, allow for easy separation, isolation, quantification and visualization of low Reynolds number  
138 cycle-invariant transient flow instabilities, based on any signal applicable to all spatial dimensions.

## 139 6. Conflict of interest statement

140 The authors have no conflicts of interest to declare.

## 141 7. Acknowledgment

142 Computations were performed on the GPC supercomputer at the SciNet (Loken et al., 2010) HPC  
143 Consortium. SciNet is funded by: the Canada Foundation for Innovation under the auspices of Compute  
144 Canada; the Government of Ontario; Ontario Research Fund - Research Excellence; and the University of  
145 Toronto. The study was supported by The Research Council of Norway through a Centres of Excellence  
146 grant to the Center for Biomedical Computing at Simula Research Laboratory, project number 179578.  
147 DAS also acknowledges salary support of a Heart & Stroke Foundation Mid-Career Investigator award. CC,  
148 DG, FM, UM and DAS acknowledge the partial support of the Joint Project of the Internationalization of  
149 research 2014 from Compagnia di San Paolo and Politecnico di Torino.

## 150 8. References

- 151 Aneurisk-Team, 2012. AneuriskWeb project website, <http://ecm2.mathcs.emory.edu/aneuriskweb>. Web Site.
- 152 Antiga, L., Piccinelli, M., Botti, L., Ene-Iordache, B., Remuzzi, A., Steinman, D. A., 2008. An image-based  
153 modeling framework for patient-specific computational hemodynamics. *Medical & biological engineering*  
154 *& computing* 46 (11), 1097–1112.
- 155 Bozzetto, M., Ene-Iordache, B., Remuzzi, A., 2015. Transitional flow in the venous side of patient-specific  
156 arteriovenous fistulae for hemodialysis. *Annals of biomedical engineering*, 1–14.
- 157 Chnafa, C., Mendez, S., Nicoud, F., 2014. Image-based large-eddy simulation in a realistic left heart. *Com-*  
158 *puters & Fluids* 94, 173–187.
- 159 Davies, P. F., Remuzzi, A., Gordon, E. J., Dewey, C. F., Gimbrone, M. A., 1986. Turbulent fluid shear  
160 stress induces vascular endothelial cell turnover in vitro. *Proceedings of the National Academy of Sciences*  
161 83 (7), 2114–2117.
- 162 Ferguson, G. G., Nov. 1970. Turbulence in human intracranial saccular aneurysms. *Journal of Neurosurgery*  
163 33 (5), 485–97.
- 164 Fry, D. L., 1968. Acute vascular endothelial changes associated with increased blood velocity gradients.  
165 *Circulation* 22 (2), 165–197.
- 166 Gallo, D., Steinman, D. A., Morbiducci, U., 2016. Insights into the co-localization of magnitude-based versus  
167 direction-based indicators of disturbed shear at the carotid bifurcation. *Journal of biomechanics*.

- 168 Gelfand, B. D., Epstein, F. H., Blackman, B. R., 2006. Spatial and spectral heterogeneity of time-varying  
169 shear stress profiles in the carotid bifurcation by phase-contrast MRI. *Journal of Magnetic Resonance*  
170 *Imaging* 24 (6), 1386–1392.
- 171 Grinberg, L., Yakhot, A., Karniadakis, G. E., 2009. Analyzing transient turbulence in a stenosed carotid  
172 artery by proper orthogonal decomposition. *Annals of biomedical engineering* 37 (11), 2200–2217.
- 173 Khan, M., Valen-Sendstad, K., Steinman, D., 2015. Narrowing the expertise gap for predicting intracranial  
174 aneurysm hemodynamics: impact of solver numerics versus mesh and time-step resolution. *American*  
175 *Journal of Neuroradiology* 36 (7), 1310–1316.
- 176 Ku, D. N., Giddens, D. P., Zarins, C. K., Glagov, S., 1985. Pulsatile flow and atherosclerosis in the hu-  
177 man carotid bifurcation. positive correlation between plaque location and low oscillating shear stress.  
178 *Arteriosclerosis, Thrombosis, and Vascular Biology* 5 (3), 293–302.
- 179 Kurokawa, Y., Abiko, S., Watanabe, K., 1994. Noninvasive detection of intracranial vascular lesions by  
180 recording blood flow sounds. *Stroke* 25 (2), 397–402.
- 181 Loken, C., Gruner, D., Groer, L., Peltier, R., Bunn, N., Craig, M., Henriques, T., Dempsey, J., Yu, C.-H.,  
182 Chen, J., et al., 2010. Scinet: lessons learned from building a power-efficient top-20 system and data  
183 centre. In: *Journal of Physics: Conference Series*. Vol. 256(1). IOP Publishing, p. 012026.
- 184 Malek, A. M., Alper, S., Izumo, S., 1999. Hemodynamic Shear Stress and Its Role in Atherosclerosis. *JAMA*  
185 282 (21), 2035–2042.
- 186 Morbiducci, U., Kok, A. M., Kwak, B. R., Stone, P. H., Steinman, D. A., Wentzel, J. J., et al., 2016.  
187 Atherosclerosis at arterial bifurcations: evidence for the role of haemodynamics and geometry. *Thrombosis*  
188 *and haemostasis* 115 (3), 484–492.
- 189 Mortensen, M., Valen-Sendstad, K., 2015. Oasis: A high-level/high-performance open source navier–stokes  
190 solver. *Computer Physics Communications* 188, 177–188.
- 191 Nerem, R., Seed, W., Wood, N., 1972. An experimental study of the velocity distribution and transition to  
192 turbulence in the aorta. *Journal of Fluid Mechanics* 52 (01), 137–160.
- 193 Peiffer, V., Sherwin, S. J., Weinberg, P. D., 2013. Computation in the rabbit aorta of a new metric–the  
194 transverse wall shear stress–to quantify the multidirectional character of disturbed blood flow. *Journal of*  
195 *Biomechanics* 46 (15), 2651–2658.
- 196 Poelma, C., Watton, P. N., Ventikos, Y., 2015. Transitional flow in aneurysms and the computation of  
197 haemodynamic parameters. *Journal of The Royal Society Interface* 12 (105), 20141394.
- 198 Pope, S. B., 2000. *Turbulent Flows*. Cambridge University Press.

- 199 Roach, M. R., Scott, S., Ferguson, G. G., 1972. The hemodynamic importance of the geometry of bifurcations  
200 in the circle of Willis (glass model studies). *Stroke* 3 (3), 255–67.
- 201 Simo, J., Armero, F., 1994. Unconditional stability and long-term behavior of transient algorithms for the in-  
202 compressible navier-stokes and euler equations. *Computer Methods in Applied Mechanics and Engineering*  
203 111 (1), 111–154.
- 204 Taylor, C. A., Steinman, D. A., 2010. Image-based modeling of blood flow and vessel wall dynamics: appli-  
205 cations, methods and future directions. *Annals of biomedical engineering* 38 (3), 1188–1203.
- 206 Valen-Sendstad, K., Mardal, K.-A., Mortensen, M., Reif, B. A. P., Langtangen, H. P., 2011. Direct Numerical  
207 Simulation of Transitional Flow in a Patient-Specific Intracranial Aneurysm. *Journal of Biomechanics*  
208 44 (16), 2826–2832.
- 209 Valen-Sendstad, K., Mardal, K.-A., Steinman, D. A., 2013. High-resolution CFD detects high-frequency  
210 velocity fluctuations in bifurcation, but not sidewall, aneurysms. *Journal of Biomechanics* 46 (2), 402–407.
- 211 Valen-Sendstad, K., Piccinelli, M., KrishnankuttyRema, R., Steinman, D. A., 2015. Estimation of inlet flow  
212 rates for image-based aneurysm cfd models: Where and how to begin? *Annals of biomedical engineering*  
213 43 (6), 1422–1431.
- 214 Valen-Sendstad, K., Piccinelli, M., Steinman, D. A., 2014. High-resolution computational fluid dynamics  
215 detects flow instabilities in the carotid siphon: Implications for aneurysm initiation and rupture? *Journal*  
216 *of biomechanics* 47 (12), 3210–3216.
- 217 Valen-Sendstad, K., Steinman, D. A., 2014. Mind the gap: Impact of CFD solution strategy on prediction  
218 of intra-cranial aneurysm hemodynamics and rupture status. *AJNR. American Journal of Neuroradiology*  
219 35 (3), 536–543, commentary, 544-545.
- 220 Varble, N., Xiang, J., Lin, N., Levy, E., Meng, H., 2016. Flow instability detected by high-resolution compu-  
221 tational fluid dynamics in fifty-six middle cerebral artery aneurysms. *Journal of biomechanical engineering*  
222 138 (6), 061009.
- 223 Yagi, T., Sato, A., Shinke, M., Takahashi, S., Tobe, Y., Takao, H., Murayama, Y., Umezu, M., 2013. Exper-  
224 imental insights into flow impingement in cerebral aneurysm by stereoscopic particle image velocimetry:  
225 transition from a laminar regime. *Journal of The Royal Society Interface* 10 (82).
- 226 Zajac, J., Eriksson, J., Dyverfeldt, P., Bolger, A. F., Ebberts, T., Carlhäll, C.-J., 2015. Turbulent kinetic  
227 energy in normal and myopathic left ventricles. *Journal of Magnetic Resonance Imaging* 41 (4), 1021–1029.