Electronic Supplementary Information (ESI) for "Matrix-dependent adhesion of vascular and valvular endothelial cells in microchannels"

Theory

For fully-developed laminar flow through a microchannel of rectangular cross-section, an analytical solution of the velocity profile has been derived. Shah and London[1] have presented both the exact solution involving Fourier series expansions, as well as a simple approximation to the velocity profile originally proposed by Purday. Because this approximation is in excellent agreement with classical experimental results, and is much easier to compute, we used it to estimate maximum velocity at the midplane of the microchannels, and shear stress on the microchannel surface.

For a microchannel of half-width $a = w/2$, and half-height $b = h/2$, the laminar velocity profile through a rectangular cross-section, as shown in Figure 1b of the main text, can be approximated by:

$$\frac{u}{u_m} = \left(\frac{m+1}{m}\right)\left(\frac{n+1}{n}\right)\left[1-\left(\frac{y}{b}\right)^n\right]\left[1-\left(\frac{z}{a}\right)^m\right] \tag{E.1}$$

and

$$\frac{u_{\max}}{u_m} = \left(\frac{m+1}{m}\right)\left(\frac{n+1}{n}\right) \tag{E.2}$$

where u, u_m, and u_{max} are the axial, mean, and maximum velocities, respectively, and m and n are empirical parameters. Wall shear stress on the bottom surface is given by

$$\tau_w = \mu \frac{du}{dy} \tag{E.3}$$

We differentiate Eq. (E.1) with respect to y and substitute $y = -b$ to obtain:

$$\frac{du}{dy} = u_m \left(\frac{m+1}{m}\right)\left(\frac{n+1}{n}\right)\left(\frac{n}{b}\right)\left[1-\left(\frac{z}{a}\right)^m\right] \tag{E.4}$$

Recognizing that $u_m = Q/wh$ and $b = h/2$, where Q is the flow rate, we can substitute Eq. (E.4) into (E.3) and simplify to obtain

$$\tau_w = \frac{2\mu Q}{wh^2}\left(\frac{m+1}{m}\right)(n+1) \tag{E.5}$$

at $z = 0$ (i.e. center of channel width).

For aspect ratio $\alpha = h/w < 1/3$, $m = 1.7 + 0.5\alpha^{-1.4}$ and $n = 2$. Channel dimensions were measured to be $h = 58.5 \pm 4.2$ μm and $w = 516 \pm 6$ μm, which yields $\alpha = 0.113$, $m = 12.24$, and $u_{max}/u_m = 1.623$. This is ~8% larger than $u_{max}/u_m = 1.5$ for the parallel plate approximation. Also, substitution of m and n into Eq. (E.5) yields

$$\tau_w = \frac{6\mu Q}{wh^2}\left(\frac{m+1}{m}\right) = 1.082 \cdot \frac{6\mu Q}{wh^2} \tag{E.6}$$

Again, as expected, the shear stress is ~8% larger than for the parallel plate approximation of $\tau_w = 6\mu Q / wh^2$. For $\mu = 0.72 \times 10^{-3}$ kg/m·s, the shear stresses applied in the channels were 11, 110, and 220 dyn/cm^2.

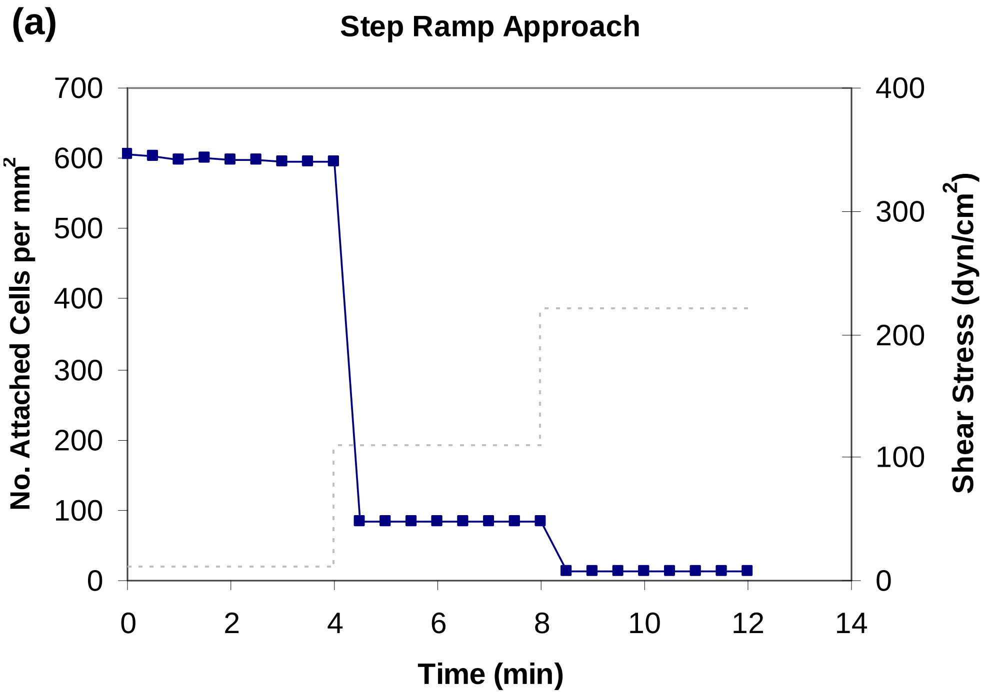
Flow Characterization

As described in the main text, particle streak velocimetry[2] was used to measure velocities in each microchannel. Flow rates of 1.2 mL/hr and 2.4 mL/hr were chosen such that measurable lengths of sufficiently bright streaklines could be obtained. At higher flow rates, streaklines spanned more than 50% of the viewfield even with the shortest possible exposure time, and therefore could not be used as an accurate measure. Five separate images were collected per microchannel, all at $x = 15$ mm from the start of the main channel section. In these velocimetry experiments, measured maximum velocities were u_{max} = 2.38 ± 0.19 mm/s for flow rate of Q = 1.2 mL/hr, and u_{max} = 4.55 ± 0.38 mm/s for Q = 2.4 mL/hr, less than 10% variability between channels within the same network. Measured maximum velocities were also consistent with theoretical predictions since Q = 1.2 mL/hr (or 0.15 mL/hr per channel) equated to u_m = 1.38 mm/s. Since $\underline{u_{max}}/u_m$ = 1.62, we have u_{max} = 2.24 mm/s, or roughly 6% difference with experiment. For Q = 2.4 mL/hr, theory predicted u_{max} = 4.48 mm/s, or less than 2% difference.

We considered the possible deformation of PDMS due to pressure-driven flow as discussed by Gervais et al.,[3] and we assessed whether the deformation experienced under our experimental conditions had a significant effect on the measured velocities and the shear stress. For a conservative estimate of Young's modulus of E = 2 MPa for PDMS cured at a 10:1 base/curing agent ratio,[3, 4] an applied flow rate of Q = 2.4 mL/hr resulted in less than 0.1% difference in the mean velocity from the beginning (x = 0) to the end (x = 30 mm) of the microchannel. Furthermore, at the highest flow rate used in the shear assay of Q = 240 mL/hr, mean velocity was predicted to differ by only 7.5% between ends of the channel. This confirms that the experimental conditions used, both for the velocimetry experiments and for the shear assay, were not significantly affected by PDMS deformation, and that there was good uniformity in shear stress from one end of the microchannel to the other.

Complementary Experiments – Dynamics of Cell Detachment

See Figure E.1 below.



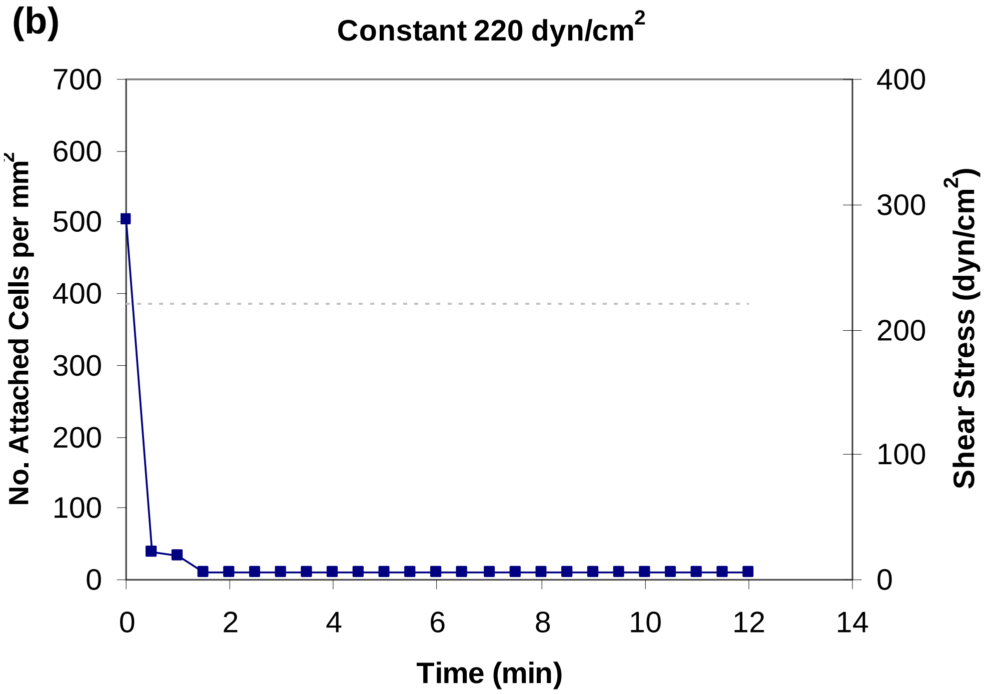


Figure E.1. Intermediate timepoint experiments for examining dynamics of cell detachment. PAVECs on FN at 50 μg/mL were used in both tests. Images were taken every 30 seconds over the 12-minute shear period. Squares = number of attached cells; filled area = shear stress level. Dotted line = shear stress applied. (a) Step ramp approach using 11, 110, and 220 dyn/cm^2 as in the experiments presented in the main text. (b) Constant 220 dyn/cm^2 applied for entire 12 minutes. Results confirm previous observations that cells detach abruptly upon exposure to each shear level.

References

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2. D. Sinton, Microscale Flow Visualization, *Microfluid Nanofluid*, 2004, 1, 2-21.
3. T. Gervais, J. El-Ali, A. Gunther and K. F. Jensen, Flow-Induced Deformation of Shallow Microfluidic Channels, *Lab Chip*, 2006, 6, 500-507.
4. D. S. Gray, J. Tien and C. S. Chen, Repositioning of Cells by Mechanotaxis on Surfaces with Micropatterned Young's Modulus, *J Biomed Mater Res A*, 2003, 66A, 605-614.