Supplementary Information for

A Microfluidic Device for Passive Separation of Platelet-Rich Plasma from Whole Blood

Pablo E. Guevara-Pantoja ^a, Yara Alvarez-Braña ^{a b}, Jon Mercader Ruiz ^{a c}, Fernando Benito-Lopez ^b, Lourdes Basabe-Desmonts ^{a d}

- Microfluidics Cluster UPV/EHU, BIOMICs Microfluidics Group, Lascaray Research Center, University of the Basque Country UPV/EHU, 01006 Vitoria-Gasteiz, Spain.
- ^b Microfluidics Cluster UPV/EHU, Analytical Microsystems & Materials for Lab-ona-Chip (AMMa-LOAC) Group, University of the Basque Country UPV/EHU, Leioa, Spain.
- ^c Advanced Biological Therapy Unit (UTBA), Hospital Vithas Vitoria, Vitoria-Gasteiz, Spain.
- ^d Basque Foundation of Science, IKERBASQUE, Bilbao, Spain.



Figure S1. Fabrication and assembly of a chip for PRP separation. (a) Cutting and engraving of PMMA layers with a laser and washing with water and soap. (b) Bonding of the hydrophilic layer and the PMMA layer with the trenches. Manual roller is used to ensure good adhesion. (c) Bonding of the double-sided PSA with the PMMA cover. Manual roller is used to ensure good adhesion. (d) Bonding of PMMA layers. (e) Placement of tubing and application of adhesive.

Microfluidic passive/active devices for Platelets separation									
Туре	No.	Method	Input blood	Purity (PTL/other cells)	Throughput	PRP yield (in/out)	Platelet activation test	Fabrication method	Reference
Passive	0	This work	Whole blood	92%	12.5 µL min ⁻¹	2folds	Yes 8.2%	Laser-cut PMIMA layers.	
	1	Inertial	Diluted	80%	1 mLmin ⁻¹	100 folds relative to other cells	No	standard soft lithography	[1] Di Carlo D, Edd JF, Irimia D, Tompkins RG, Toner M (2008) Equilibrium separation and filtration of particles using differential inertial focusing. Anal Chem 80(6):2204-2211
	2	Hydrophoretic	Diluted	82.8%	2×10^5 cells s ⁻¹	0.41 folds	No	two-step photolithography	[2] Choi S, Ku T, Song S, Choi C, Park JK (2011) Hydrophoretic high-throughput selection of platelets in physiological shear-stress range. Lab Chip 11(3):413-418
	3	Deterministic Lateral Displacement	Diluted	N/D	1000 cells s ⁻¹	0.7folds	No	standard soft lithography	[3] Li N, Kamei DT, Ho CM (2007) On-chip continuous blood cell subtype separation by deterministic lateral displacement. In: Nano/micro engineered and molecular systems, 2007. NEMS 07. 2nd I⊞ International Conference, pp 932-936
	4	Hydrodynamic lift	Diluted	N/D	N/D	Not measured	No	standard soft lithography	[4] Geislinger TM, Eggart B, Braunmüller S, Schmid L, Franke T (2012) Separation of blood cells using hydrodynamic lift. Appl Phys Lett 100(18):183701
	5	Filtration	Whole blood	<2000 RBC/ul	1.67 mLmin ⁻¹	1.15 folds	No	Laser-cut PP layers.	[5] Ascalable, micropore, platelet rich plasma separation device. Biomed Microdevices 14(6):1095-1102
	6	Platelet margination	Whole blood	50.7%	0.4 mLmin ⁻¹	15 folds	Yes 4,5%	standard soft lithography	[6] Design Evolution and Performance Study of a Reliable Platelet-Rich Plasma Microdevice
	7	Sedimentation	Wholeblood	~100%	50 µLhr ⁻¹	Not measured	No	standard soft lithography	[7] Sand-alone self-powered integrated microfluidic blood analysis system (SIMBAS), Lab Chip 11 (2011) 845-850
	8	Platelet margination	Plasma sample	97.8%	120 µLmin ⁻¹	2.6 folds	No	standard soft lithography	[8] Blood component separation in straight microfluidic channels. Biomicrofluidics, 2023, 17(5).
	9	Platelet margination	Whole blood	25.5%	0.4 mLmin ⁻¹	8.7 folds	Yes	standard soft lithography	[9] Separation and Enrichment of Platelets from Whole Blood Using a PDMS-Based Passive Microdevice. Industrial & Engineering Chemistry Research, 2020, 59(10), 4792-4801
Active	10	Dielectrophoresis	Diluted	95%	2.2 x 10 ⁴ cells s ⁻¹	Not measured	Yes	Gass-based microfabrication with metal-polymer integration and thermal bonding	[10] Pommer MS, Zhang Y, Keerthi N, Chen D, Thomson JA, Meinhart CD, Soh HT (2008) Dielectrophoretic separation of platelets from diluted whole blood in microfluidic channels. Bectrophoresis 29(6):1213-1218
	11	Dielectrophoresis	Diluted	98.8%	134 µm s ⁻¹	0.98 folds	No	Gass microdevice with Pt electrodes, SU-8 channels, and PDMSsealing on PCB	[11] Placentini N, Mernier G, Tornay R, Penaud P (2011) Separation of platelets from other blood cells in continuous-flow by dielectrophoresis field-flow- fractionation. Biomicrofluidics 5(3):034122
	12	Surface acoustic waves	Whole blood	98%	2.7×10^4 cells s ⁻¹	0.74 folds	No	PDMSchannels in SSAW substrate along with IDTs	[12] Nam J, Lim H, Kim D, Shin S(2011) Separation of platelets from whole blood using standing surface acoustic waves in a microchannel. Lab Chip 11(19):3361-3364
	13	Acoustic separation	Whole blood	88.4% RBC/WBC removal	5mLmin ⁻¹	0.86 folds	Yes	stainless steel sheets cut by laser over a transducer	[13] Chen Y, Wu M, Ren L, Liu J, Whitley PH, Wang L, Huang TJ (2016) High-throughput acoustic separation of platelets from whole blood. Lab Chip 16(18):3466-3472
	14	Gravitational sedimentation enhanced by dielectrophoresis	Whole blood	99.98%	100 nLs ⁻¹	0.22 folds	No	PDMSsoft lithography, with sputtered electrodes on glass, a punched trench, and an MBPP membrane	[14] Amicrofluidic device to separate high-quality plasma from undiluted whole blood sample using an enhanced gravitational sedimentation mechanism, Anal Chim Acta 1239 (2023) 340641

Table S1. Microfluidic passive/active devices for Platelets separation. The works are grouped into passive and active systems. Advantages of each system are highlighted in green, disadvantages in red, and potential limitations in yellow. Active systems are marked in yellow due to their more complex operation compared to passive systems.

References

- Di Carlo D, Edd JF, Irimia D, Tompkins RG, Toner M. Equilibrium separation and filtration of particles using differential inertial focusing. Anal Chem, 2008, 80(6):2204–2211
- [2] Choi S, Ku T, Song S, Choi C, Park JK. Hydrophoretic high-throughput selection of platelets in physiological shear-stress range. Lab Chip, 2011, 11(3):413–418
- [3] Li N, Kamei DT, Ho CM. On-chip continuous blood cell subtype separation by deterministic lateral displacement. In: Nano/micro engineered and molecular systems. NEMS'07. 2nd IEEE International Conference, 2007, pp 932–936
- [4] Geislinger TM, Eggart B, Braunmüller S, Schmid L, Franke T. Separation of blood cells using hydrodynamic lift. Appl Phys Lett, 2012, 100(18):183701
- [5] A scalable, micropore, platelet rich plasma separation device. Biomed Microdevices, 2012, 14(6):1095–1102
- [6] Design Evolution and Performance Study of a Reliable Platelet-Rich Plasma Microdevice
- [7] Stand-alone self-powered integrated microfluidic blood analysis system (SIMBAS), Lab Chip, 2011, 11, 845–850
- [8] Blood component separation in straight microfluidic channels. Biomicrofluidics, 2023, 17(5).
- [9] Separation and Enrichment of Platelets from Whole Blood Using a PDMS-Based Passive Microdevice. Industrial & Engineering Chemistry Research, 2020, 59(10), 4792-4801
- [10] Pommer MS, Zhang Y, Keerthi N, Chen D, Thomson JA, Meinhart CD, Soh HT. Dielectrophoretic separation of platelets from diluted whole blood in microfluidic channels. Electrophoresis, 2008, 29(6):1213–1218
- [11] Piacentini N, Mernier G, Tornay R, Renaud P. Separation of platelets from other blood cells in continuous-flow by dielectrophoresis field-flow-fractionation. Biomicrofluidics, 2011, 5(3):034122
- [12] Nam J, Lim H, Kim D, Shin S. Separation of platelets from whole blood using standing surface acoustic waves in a microchannel. Lab Chip, 2011, 11(19):3361–3364
- [13] Chen Y, Wu M, Ren L, Liu J, Whitley PH, Wang L, Huang TJ. High-throughput acoustic separation of platelets from whole blood. Lab Chip, 2016, 16(18):3466–3472
- [14] A microfluidic device to separate high-quality plasma from undiluted whole blood sample using an enhanced gravitational sedimentation mechanism, Anal Chim Acta, 2023, 1239 340641.