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Blood sample preparation for drug monitoring

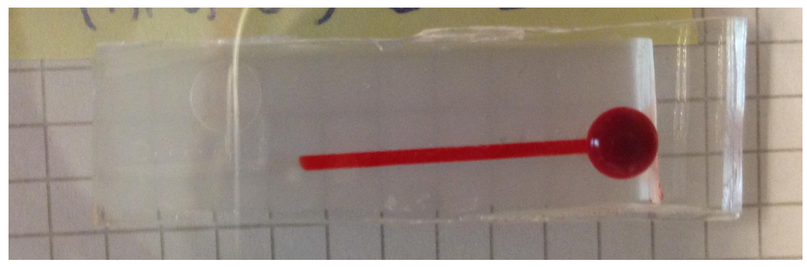
D. Forchelet, P. Renaud

Ecole Polytechnique Fédérale de Lausanne

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Introduction

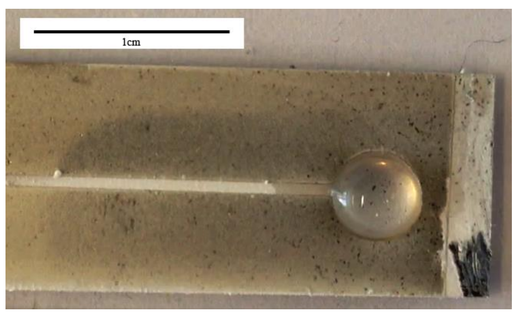
Plasma is the liquid fraction of blood samples into which blood cells are suspended. It usually accounts for more than 50% of the volume in whole blood. This fraction has an important impact in blood analysis as it contains a large variety of drugs, proteins and other biomarkers. Its extraction usually requires the use of a centrifugation machine with large volumes of blood, we propose here on-chip alternatives using microsampling from finger pricks..

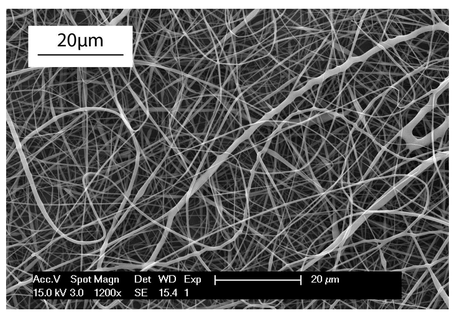


Electrospinning

Electrospinning is a method for deposition of porous mats through the application of electric field to a polymeric solution. A high voltage is applied to a drop at the end point of a nozzle, creating a protrusion and eventually a jet of polymer towards the target electrode. This polymeric fiber dries during flight and a nanofiber mat.

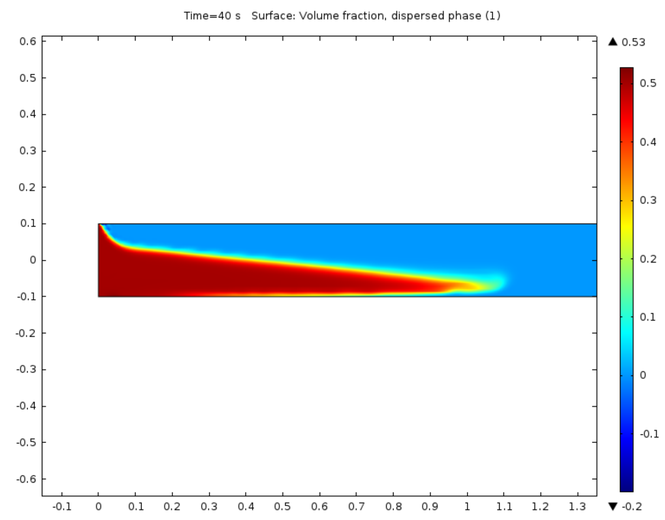
Electrospinning was used to create both hydrophilic and hydrophobic patterned structures. We propose to use this method to create paper-like microfluidic devices. Amongst which, plasma extraction through on chip cell filtration.





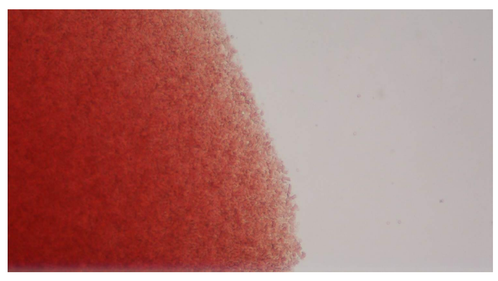
Microfluidic chip

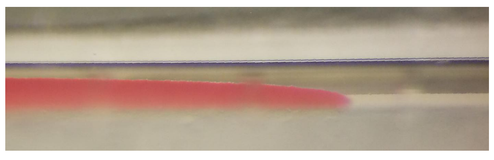
A microfluidic chip approach was developed in collaboration with DBS Systems. A device using gravitational forces in microchannels was implemented. Hemorheological differences lead to a spatial separation between the concentrated cell fraction and a clear plasma fraction. The sample preparation microfluidic device needs no separate machine to operate as capillary pressure drives the liquid in the microfluidic circuit .



Applications and results

The device contains a separation channel along which a slower cell suspension front and faster clear plasma front progress. This difference of progression speed creates a large plasma plug as the separation channel fills. This device yields a larger amount of clear plasma with low lysis of red blood cells. Volumes of up to 8µL of plasma, without any visible cells, have been extracted from 20µL whole blood samples.





In addition, to the separation channel, an ejection mechanism is present on the chip. A volume defined to 2µL is ejected from the chip by using an air bubble and capillary valve. The ejection of the plasma allows for using the generated plasma in any on-chip or off-chip operation or characterization.

Conclusion

The standard microfluidic and electrospinning platforms are promising methods for on-chip blood separation. The quality of generated plasma compared to a centrifuged reference is excellent and allows this process to be used in a large variety of point-of-care sample preparation situations. Fibrinogen was identified in the generated plasma: confirming that we are in presence of plasma not serum. Fluorescence Polarization method in HES-Sion showed a retrieval of 100% of spiked tobramycin in whole blood. Protein detection using mass spectrometry showed a similar number of identified proteins between on-chip generated plasma and reference.