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Retrospective analysis of archival tissue sections using tissue microprocessing

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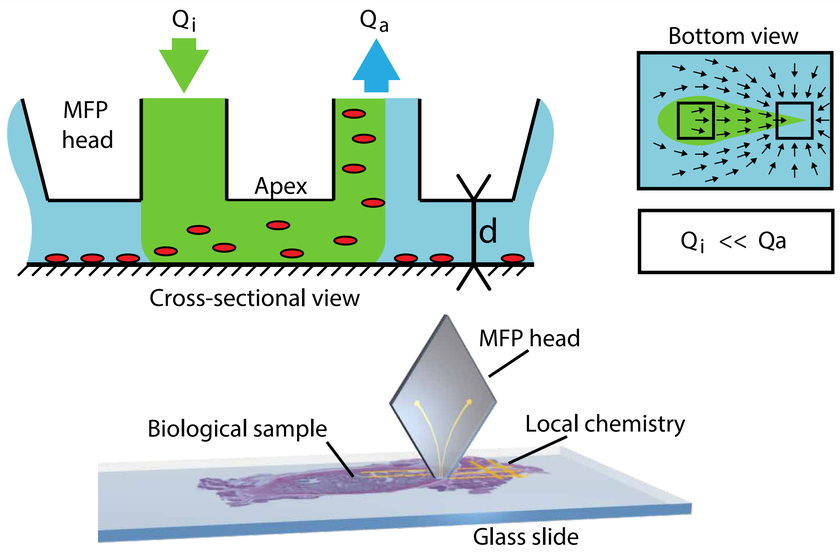
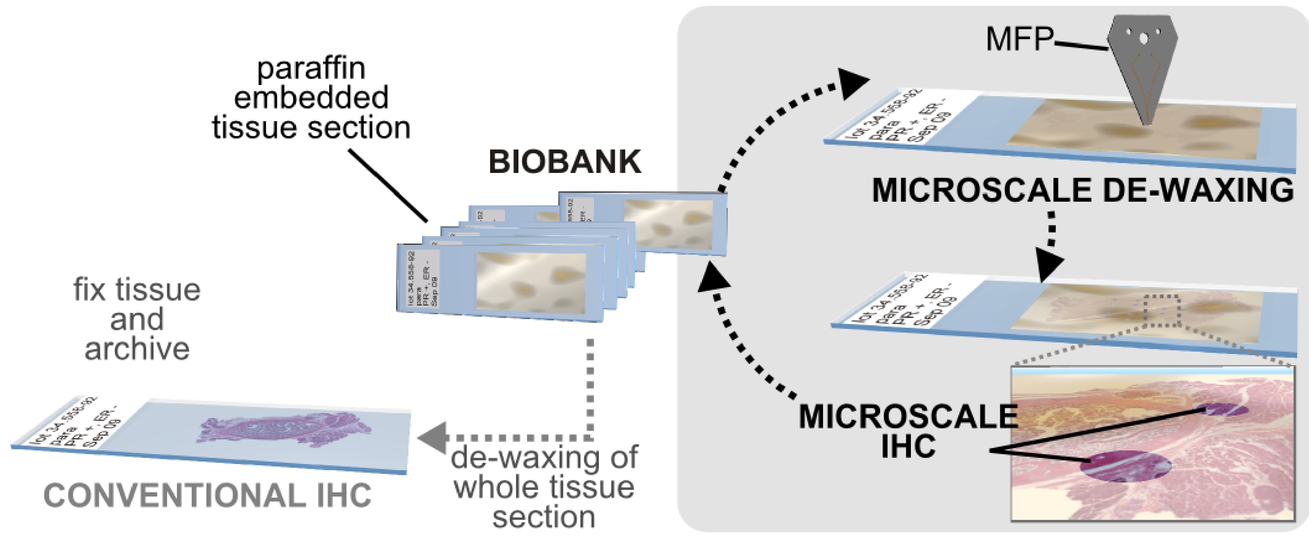
Microfluidic Probe



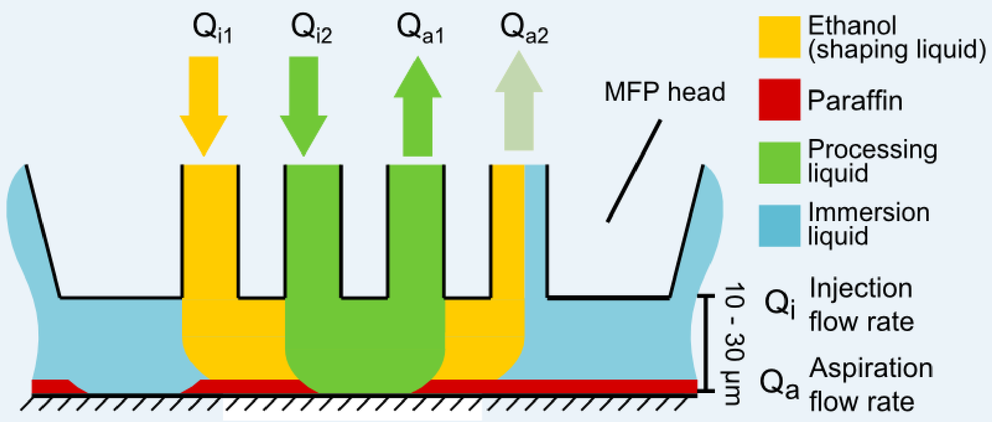
The microfluidic probe (MFP) is a non-contact, scanning technology that operates in the "open-space" [1]. The MFP allows to perform chemistry on surfaces at the micrometer length-scale by hydrodynamically confining a processing liquid within an immersion liquid [2-3].

Local de-waxing on archival tissue sections



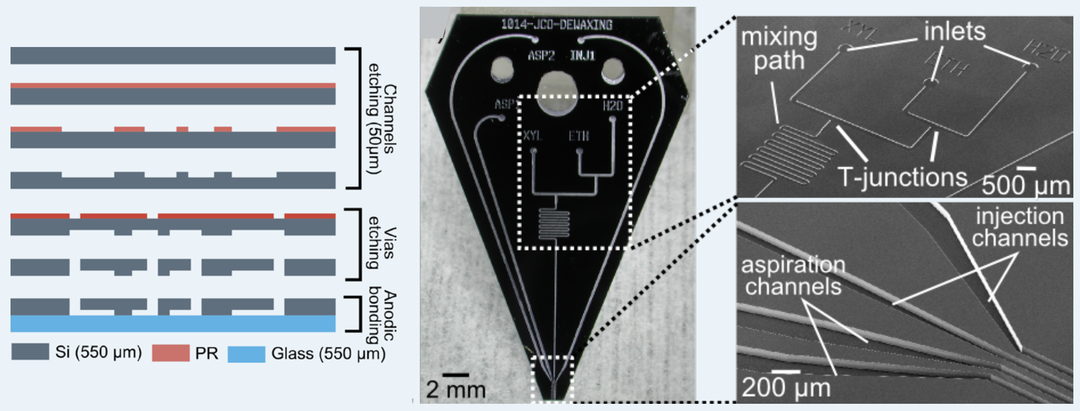
Formalin-fixed paraffin-embedded (FFPE) tissue sections are stored in biobanks and are highly valuable for biomarker validation and drug discovery. Tissue microprocessing with the MFP allows to process a fraction of the archived sample while retaining the rest for future analysis.

HFC with immiscible liquids



Paraffin removal is performed using xylene. The immiscibility of xylene and water prevents the formation of a stable HFC. To overcome this limitation, a third liquid (i.e. a ¨shaping liquid¨) is introduced via two outer apertures to shield the processing liquid (xylene) from the immersion liquid (water). [4]

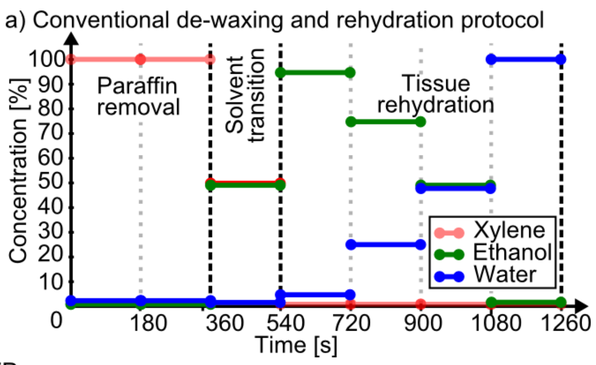
Microfabricated MFP heads

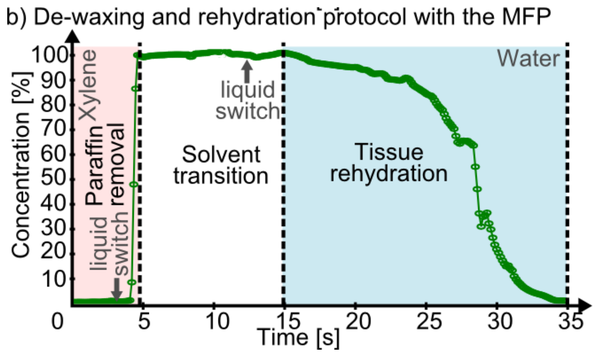


A hybrid silicon-glass MFP head with four coplanar appertures (cross-section: 50 x 50 µm) has been microfabricated. The channels are etched using deep reactive-ion etching and the silicon layer was sealed with glass using anodic bonding. The head includes two T-junctions and a mixing path to create time varying concentration gradients in the flow confinement.

Gradual rehydration of tissues

The standard de-waxing and rehydration protocol used in pathology involves successive dipping of the FFPE section in multiple solvent baths. The wax is removed on the entire tissue section. Subsequently, the sample is gradually rehydrated to avoid osmotic shocks on the membranes. The entire protocol requires more than 20 minutes.

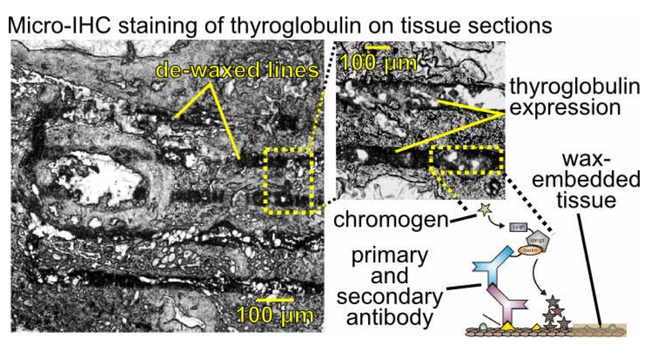




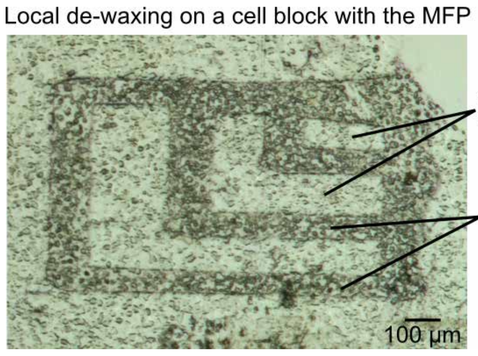
The MFP implementation of the protocol requires only 30 seconds for de-waxing and complete rehydration. This 40-fold time reduction is due to the advantageous transport phenomena at the microscale (short diffusion length, advection) that the MFP leverages.

IHC staining on de-waxed areas

De-waxing and rehydration were performed on two samples: BRAF V600E+ melanoma cell block (5 µm thick) and human thyroid tissue section (6 µm thick). The quality of the removal was assessed via hematoxylin staining and immunohistochemistry staining against thyroglobulin.



Local de-waxing on a cell block with the MFP



The results show staining and thyroglobulin expression only on de-waxed areas of the sample. This suggest that the MFP can optimize the time, resolution and content performances of the analysis of precious samples that drive new biomarker discovery in oncology.

References

[1] J. F. Cors, R. D. Lovchik, E. Delamarche and G. V. Kaigala, **Rev. Sci. Instr.**, 2014.
[2] G. V. Kaigala, R. D. Lovchik, U. Drechsler and E. Delamarche, **Langmuir**, 2012.
[3] R. D. Lovchik, G. V. Kaigala, M. Georgiadis and E. Delamarche, **Lab Chip**, 2012
[4] J. Autebert, A. Kashyap, R. D. Lovchik, E. Delamarche and G. V. Kaigala, **Langmuir**, 2014

Acknowledgments

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