Multi-color fluorescent DNA analysis in an integrated optofluidic lab-on-a-chip

C. Dongre[1], J. van Weerd[2], R. van Weeghel[2], R. Martinez Vazquez[3], R. Osellame[3], G. Cerullo[3], G.A.J. Besselink[4], H.H. van den Vlekkert[4], H.J.W.M. Hoekstra[1] and M. Pollnau[1]

[1]*Integrated Optical MicroSystems (IOMS), MESA+ Institute for Nanotechnology, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands*
Tel. +31 (0) 53 489 4449, Fax +31 (0) 53 489 3343
E-mail: C.Dongre@ewi.utwente.nl

[2] *Zebra Bioscience BV, W. Beversstraat 185, 7543 BK Enschede, The Netherlands*

[3]*Istituto di Fotonica e Nanotecnologie del CNR, Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milan, Italy*

[4]*LioniX BV, P.O. Box 456, 7500 AL Enschede, The Netherlands*

Sorting and sizing of DNA molecules within the human genome project has enabled the genetic mapping of various illnesses. By employing tiny lab-on-a-chip devices for such DNA analysis, integrated DNA sequencing and genetic diagnostics have become feasible. However, such diagnostic chips typically lack integrated sensing capability. We address this issue by combining microfluidic capillary electrophoresis with laser-induced fluorescence detection resulting in optofluidic integration towards an on-chip bio-analysis tool [1,2]. We achieve a spatial separation resolution of 12 μm, which can enable a 20-fold enhancement in electropherogram peak resolution, leading to plate numbers exceeding one million. We demonstrate a high sizing/calibration accuracy of 99% [3], and ultrasensitive fluorescence detection (limit of detection = 65 femtomolar, corresponding to merely 2-3 molecules in the excitation/detection volume) of diagnostically relevant double-stranded DNA molecules by integrated-waveguide laser excitation. Subsequently, we introduce a principle of parallel optical processing to this optofluidic lab-on-a-chip. Different sets of exclusively color-labeled DNA fragments – otherwise rendered indistinguishable by their spatio-temporal coincidence – are traced back to their origin by modulation-frequency-encoded multi-wavelength laser excitation, fluorescence detection with a color-blind photomultiplier, and Fourier-analysis decoding. As a proof of principle, fragments from independent human genomic segments, associated with genetic predispositions to breast cancer and anemia, are extracted by multiplex ligation-dependent probe amplification, and simultaneously analyzed. Such multiple yet unambiguous optical identification of biomolecules opens new horizons for "enlightened" lab-on-a-chip devices.

References:

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