Final Publishable Report – Figures

Grant Agreement number: 278204

Project acronym: CELL-O-MATIC

Project title: HIGH THROUGHPUT SYSTEMATIC SINGLE CELL GENOMICS USING MICRO/NANO-FLUIDIC CHIPS FOR EXTRACTING, PRE-ANALYSING, SELECTING AND PREPARING SEQUENCE-READY DNA

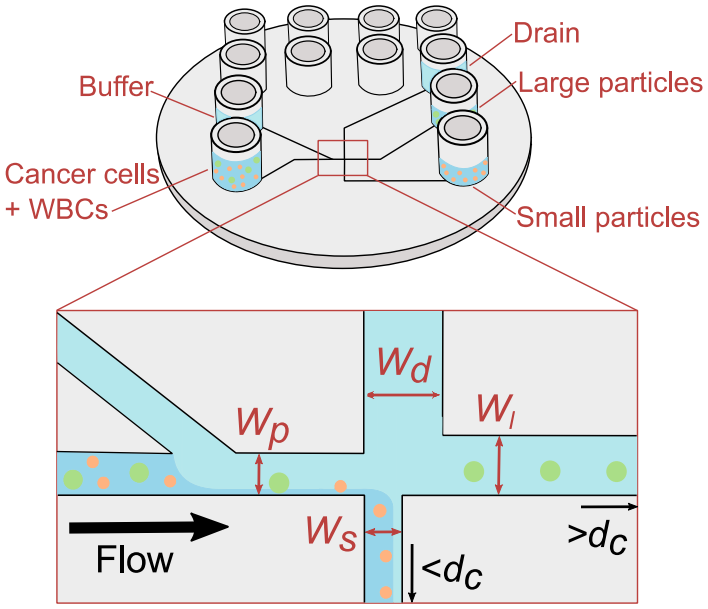


Figure 2.1: Schematic of PFF devices. Cells larger than the critical size d_c are collected in the large cell outlet.

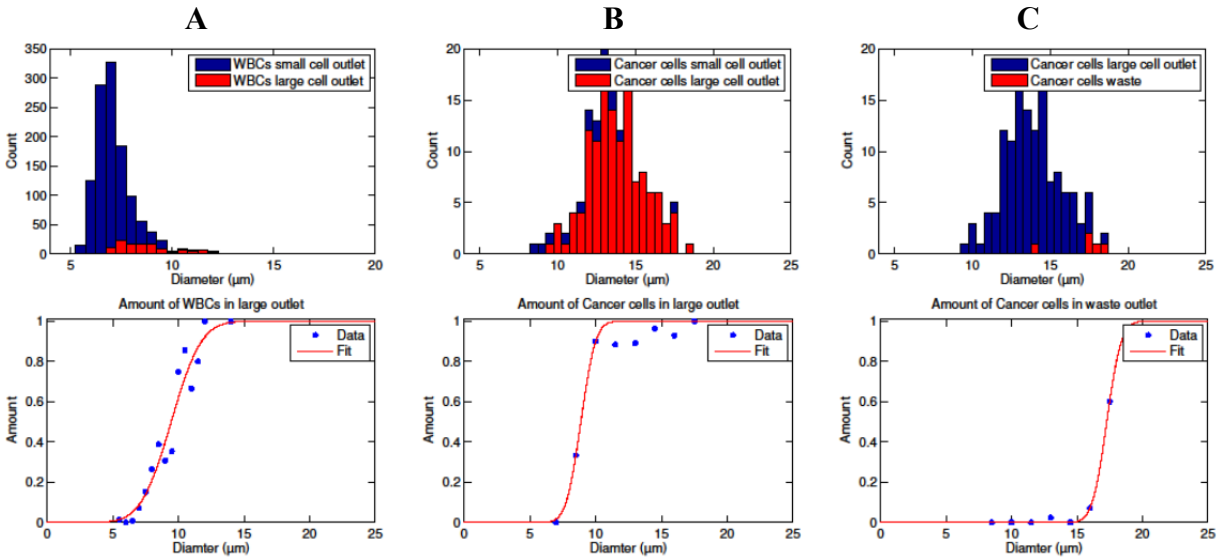


Figure 2.2: Sorting LS174T colorectal cancer cells using PFF devices. Size distribution of white blood cells in small and large outlet (A), cancer cells in small and large outlet (B), cancer cells in waste outlet (C).

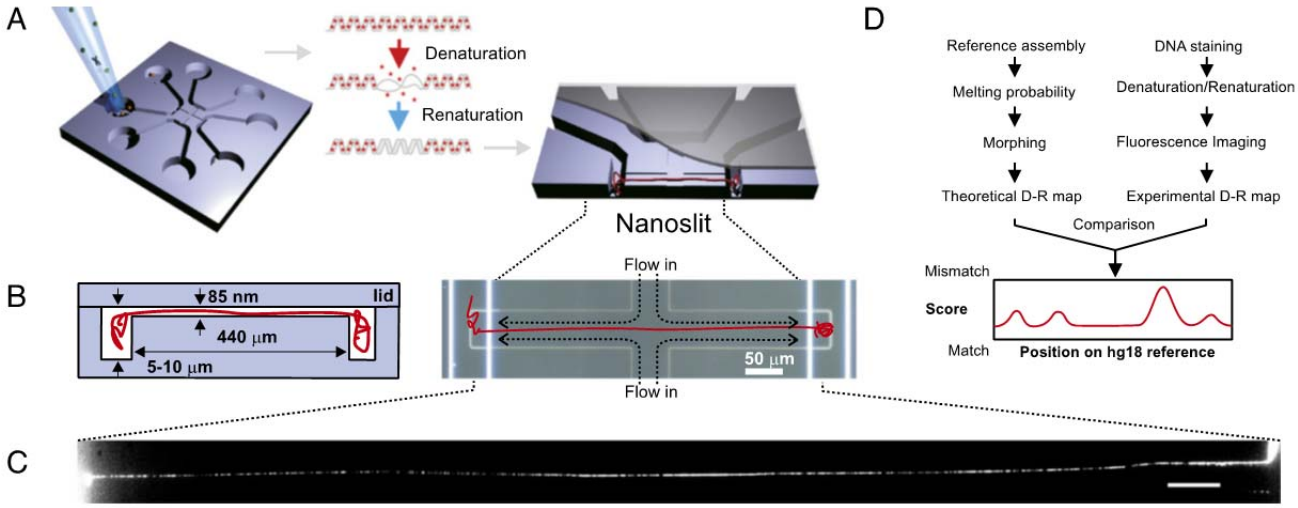


Figure 3.1: Optical mapping by denaturation-renaturation. (A) The chip is loaded with cell extract enriched in metaphase chromosomes. Stained DNA is partially denatured and renatured, creating a fluorescence pattern (DR map). (B) The inlet ports of the chip connect to 5- to 10-µm-deep microchannels for DNA handling, which feed into an 85-nm shallow nanoslit. This nanoslit effectively confines DNA molecules to 2D and stretches them by opposing fluid flows from a second, perpendicular nanoslit. A megabase pair-long DNA fragment is (B) flow-stretched and (C) imaged, and (D) its DR map is compared locally to the reference genome's (hg18); chromosomal origin and structural variations are detected as good vs. poor matches.

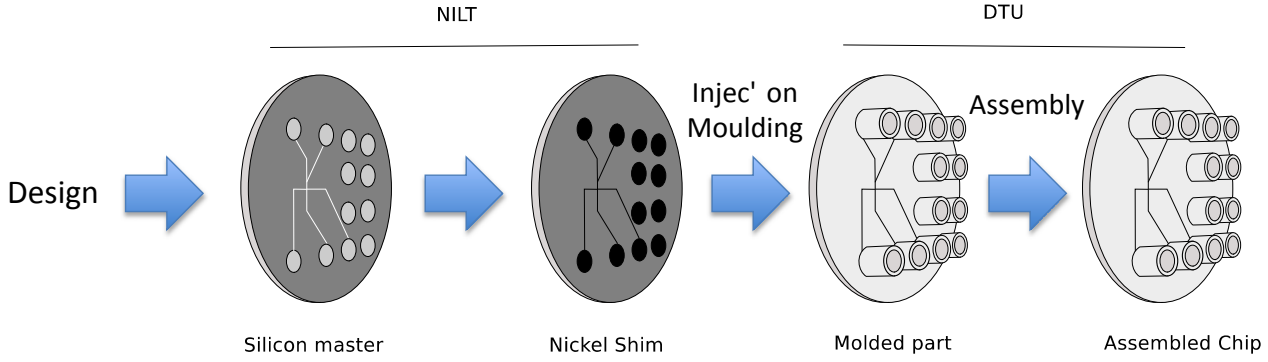


Figure 4.1: Workflow for the production of polymer lab-on-a-chip by injection moulding in Cell-O-Matic.

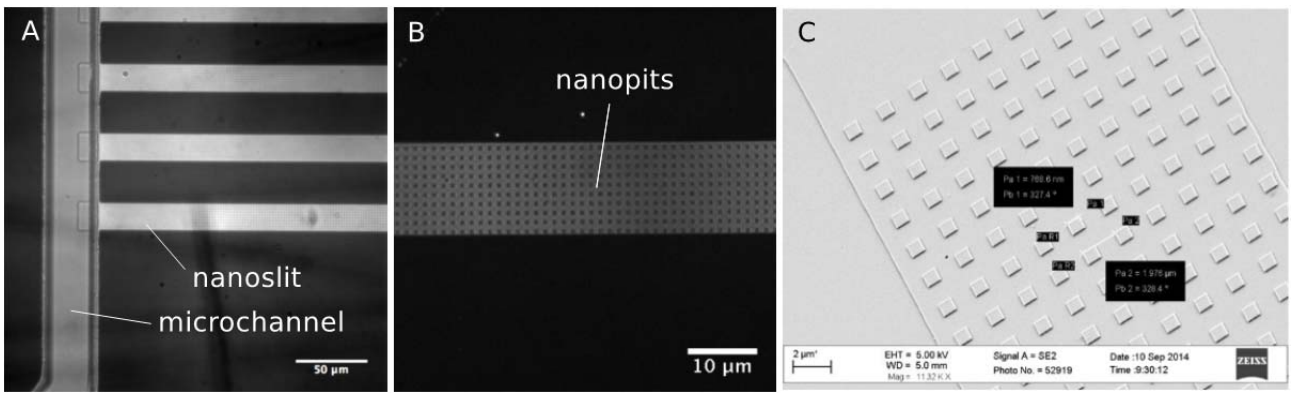


Figure 4.2: Optical microscopy images of (A) the nanofluidic device combining three levels, one microfluidics, one nanofluidics low aspect ratio (nanoslit) and a further nanofluidic level consisting of nanopits (C) electron microscopy image of the nickel shim showing the protrusions used for defining the nanopits.

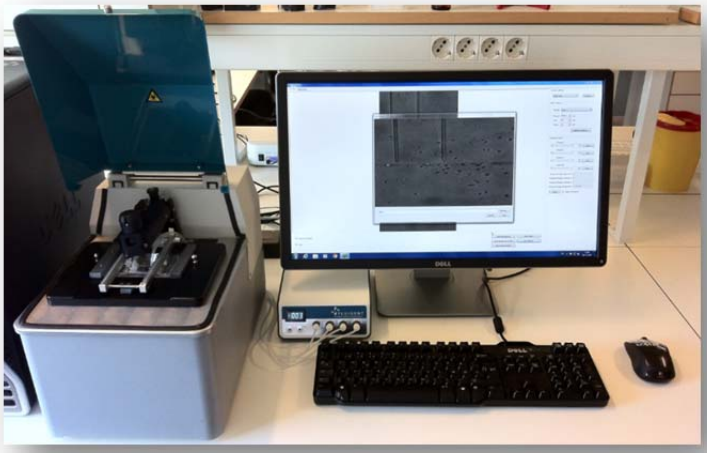


Figure 7.1: Cell-O-Matic system

Temperature control module

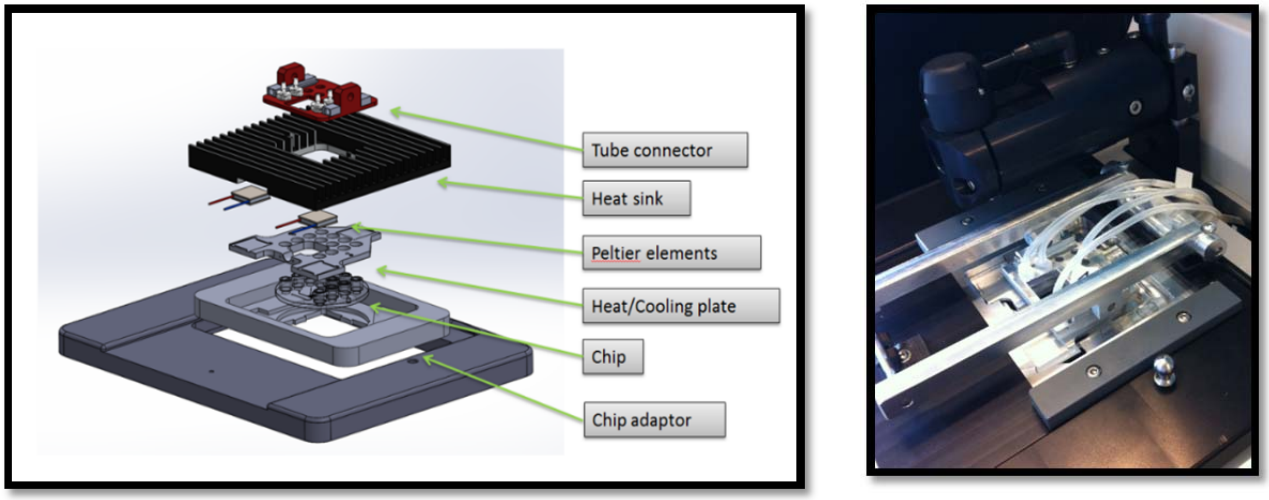


Figure 7.2 Temperature module (left) design and (right) implementation on the prototype instrument.

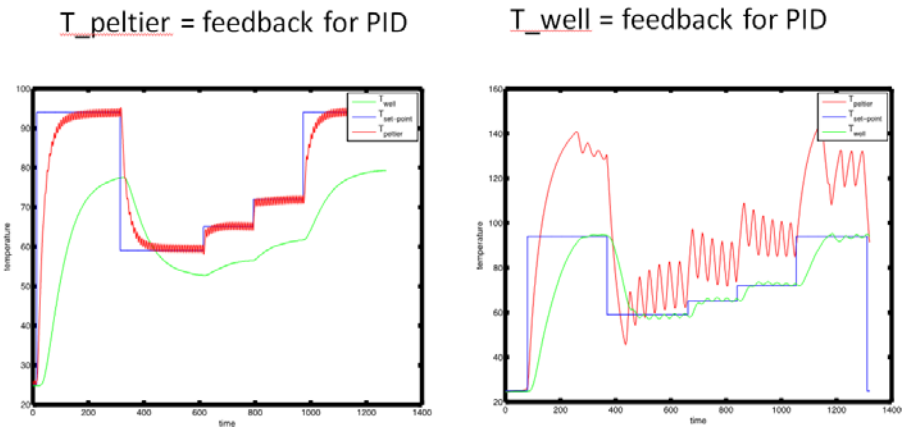


Figure 7.3 (a, b): Optimization test of temperature module: Results from Test 2: 94/59/65/72 C cycle (conducted by Rodolphe Marie, DTU Nanotech)

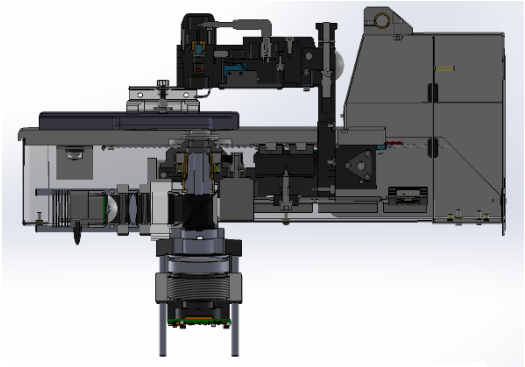


Figure 7.4: Fluorescence module design

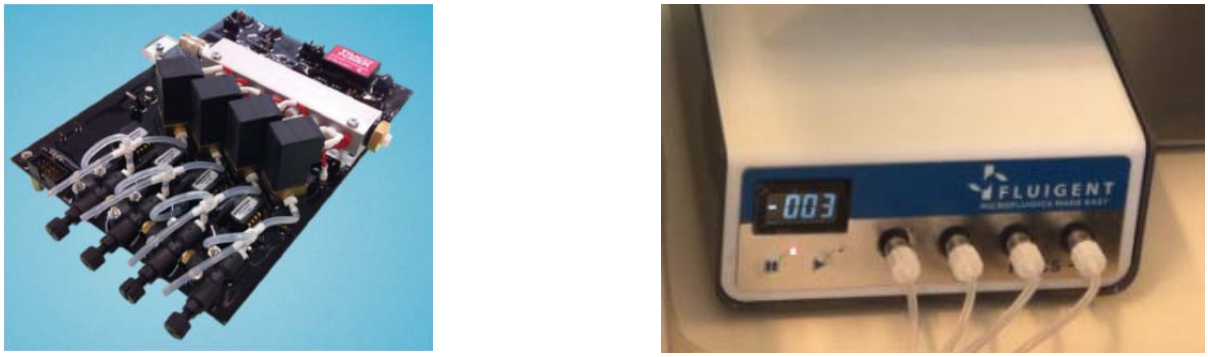


Figure 7.5. (left) OEM design and (right) Instrument of the Fluigent pressure control unit.

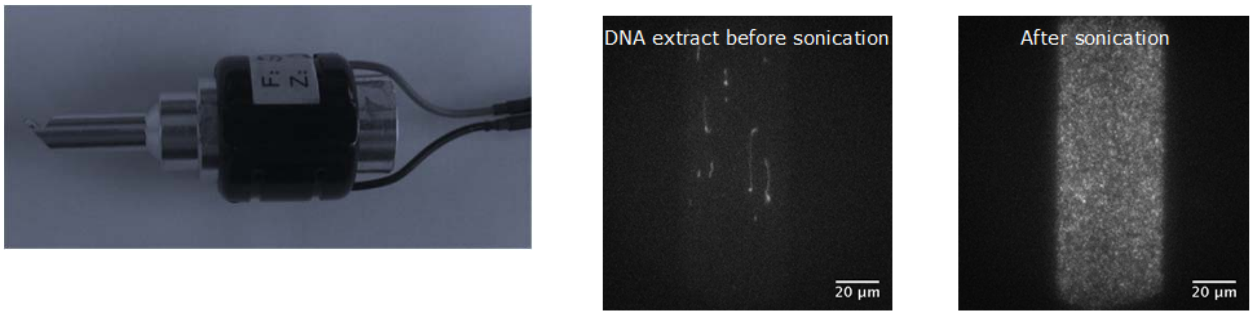


Figure 7.6. Ultrasound module. Ultrasound actuator (left) and genomic DNA fragmented by ultrasound (right).

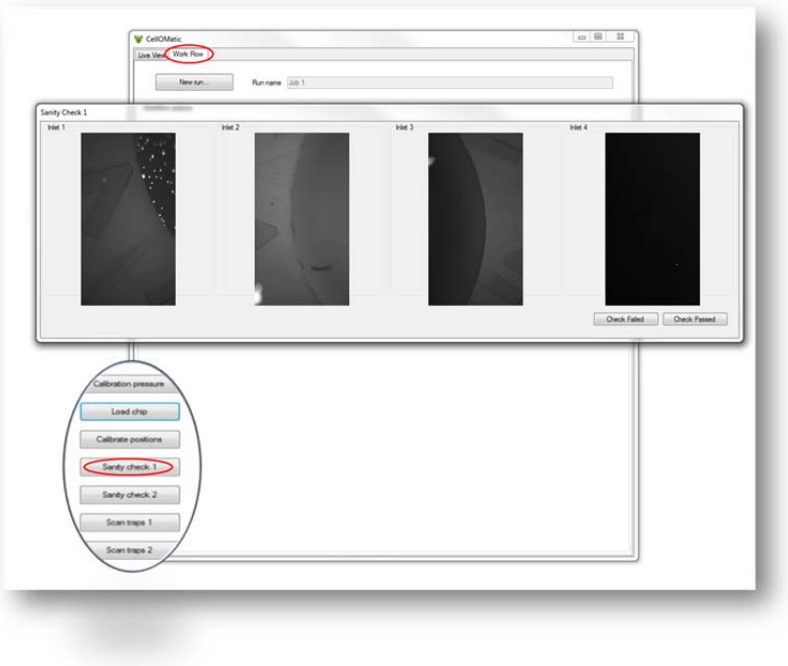


Figure 7.7: GUI - workflow view

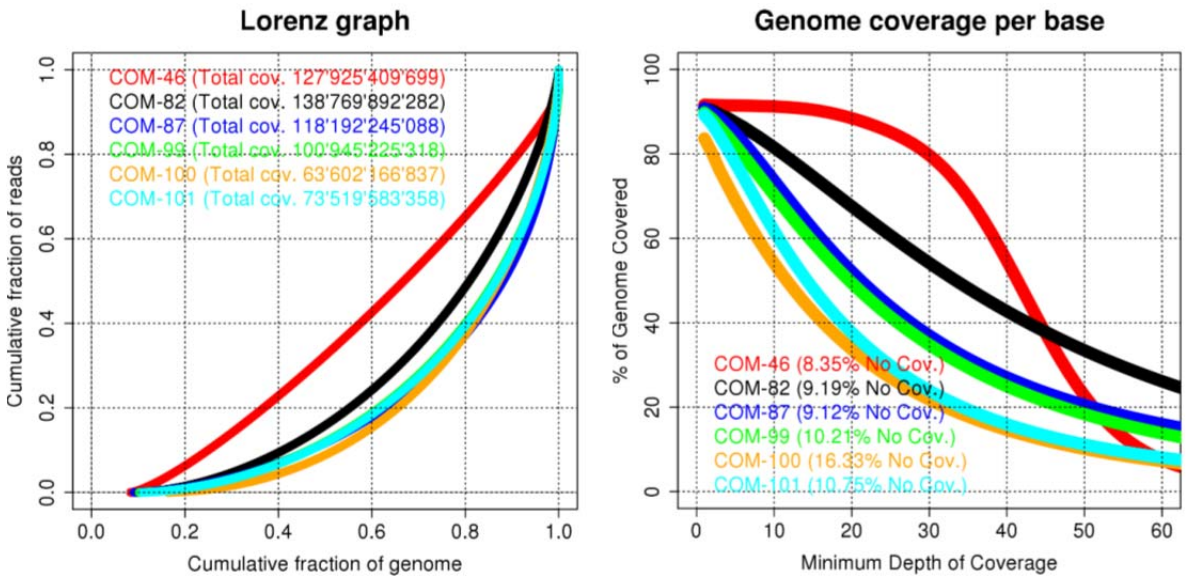


Figure 8.1: Coverage and Lorenz graph of the sequencing results for the on-chip amplified material after deeper sequencing (with COM-46 reference bulk).

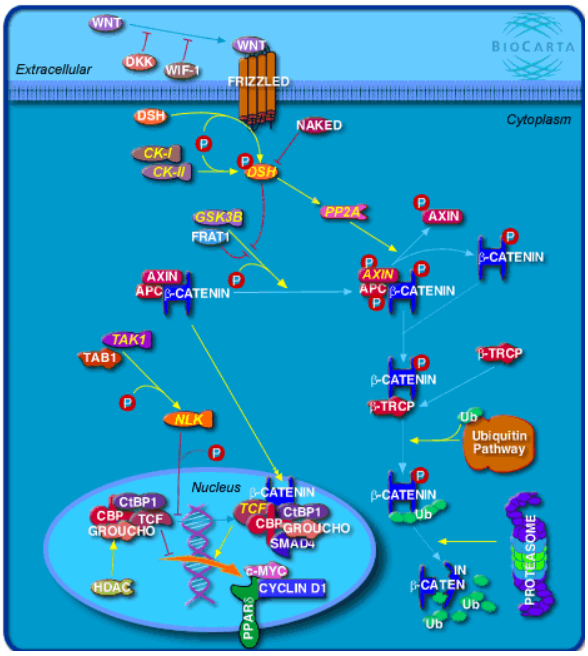
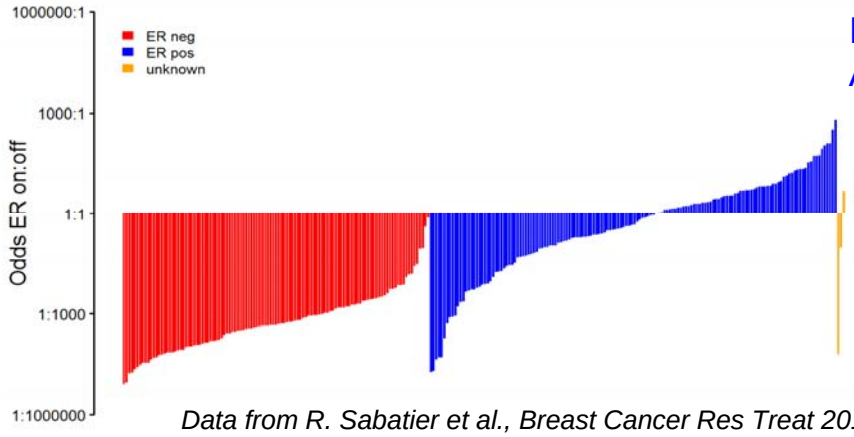


Figure 9.1: Diagram of the Wnt developmental pathway in the cell



Data from R. Sabatier et al., Breast Cancer Res Treat 2011; 126(2):407-20 [GEO data set GSE21653]

Figure 9.2: Bayesian pathway analysis of ER pathway activity in patients' samples judged to be ER+ and ER-. Note that according to this model some 50% of the ER+ cases are not ER active (for details see W. Verhaegh et al. Cancer Res 74 (2014) 2936).

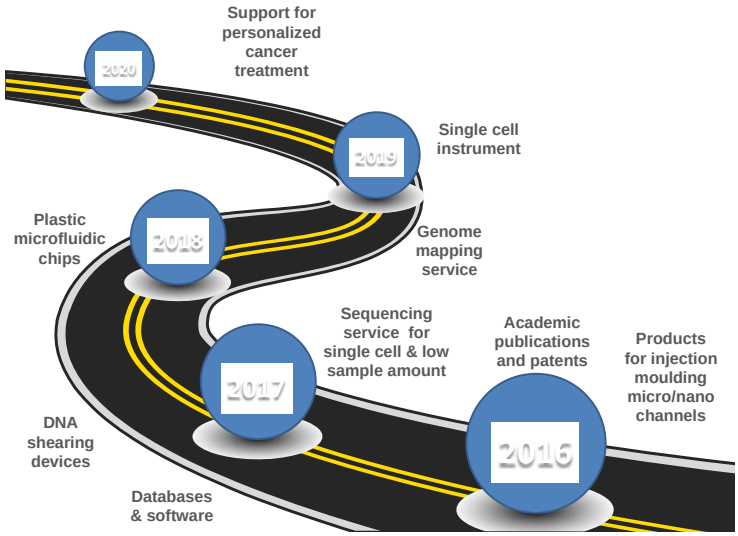


Figure 10.1: Roadmap of Cell-O-Matic outcomes