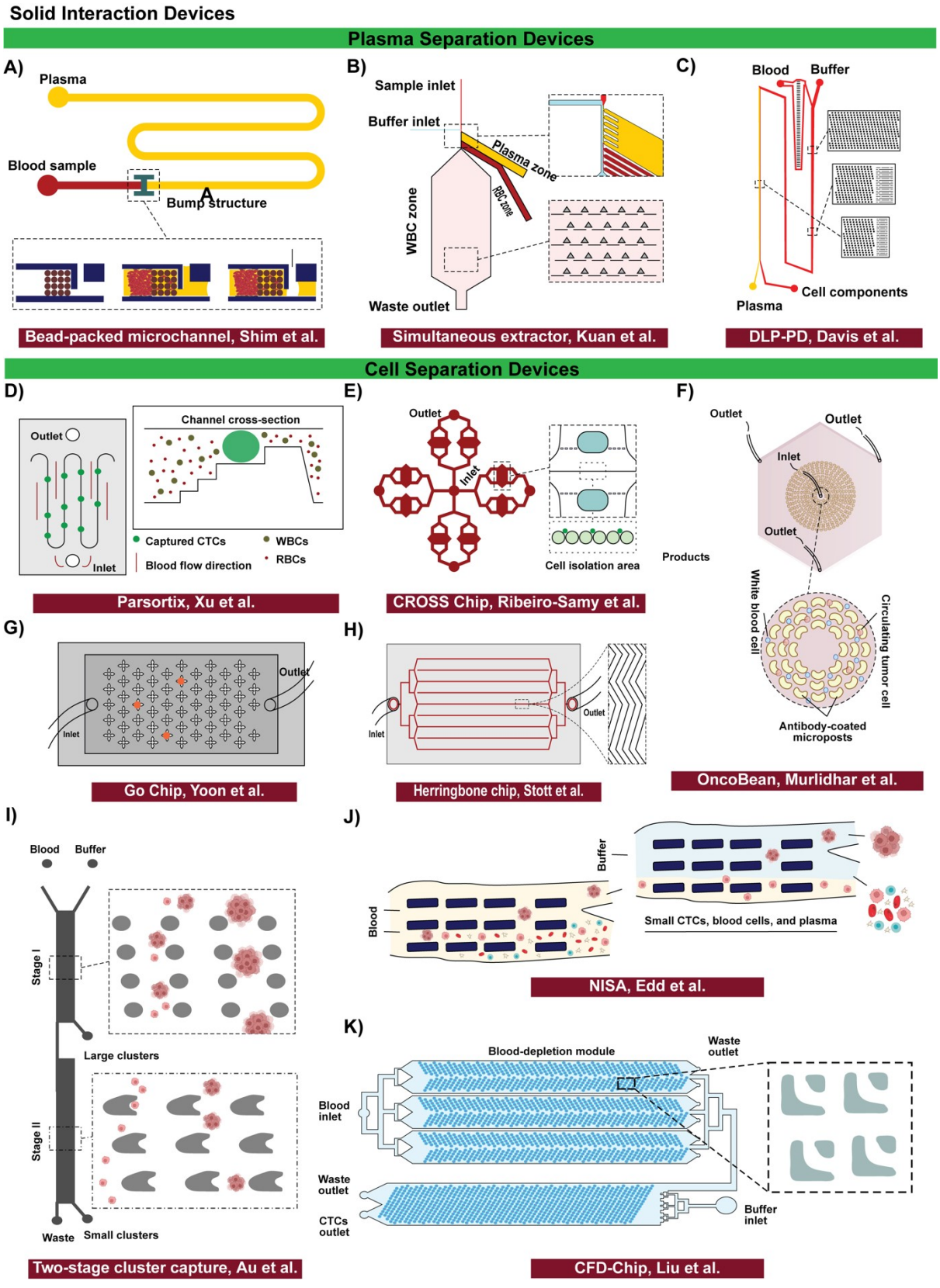
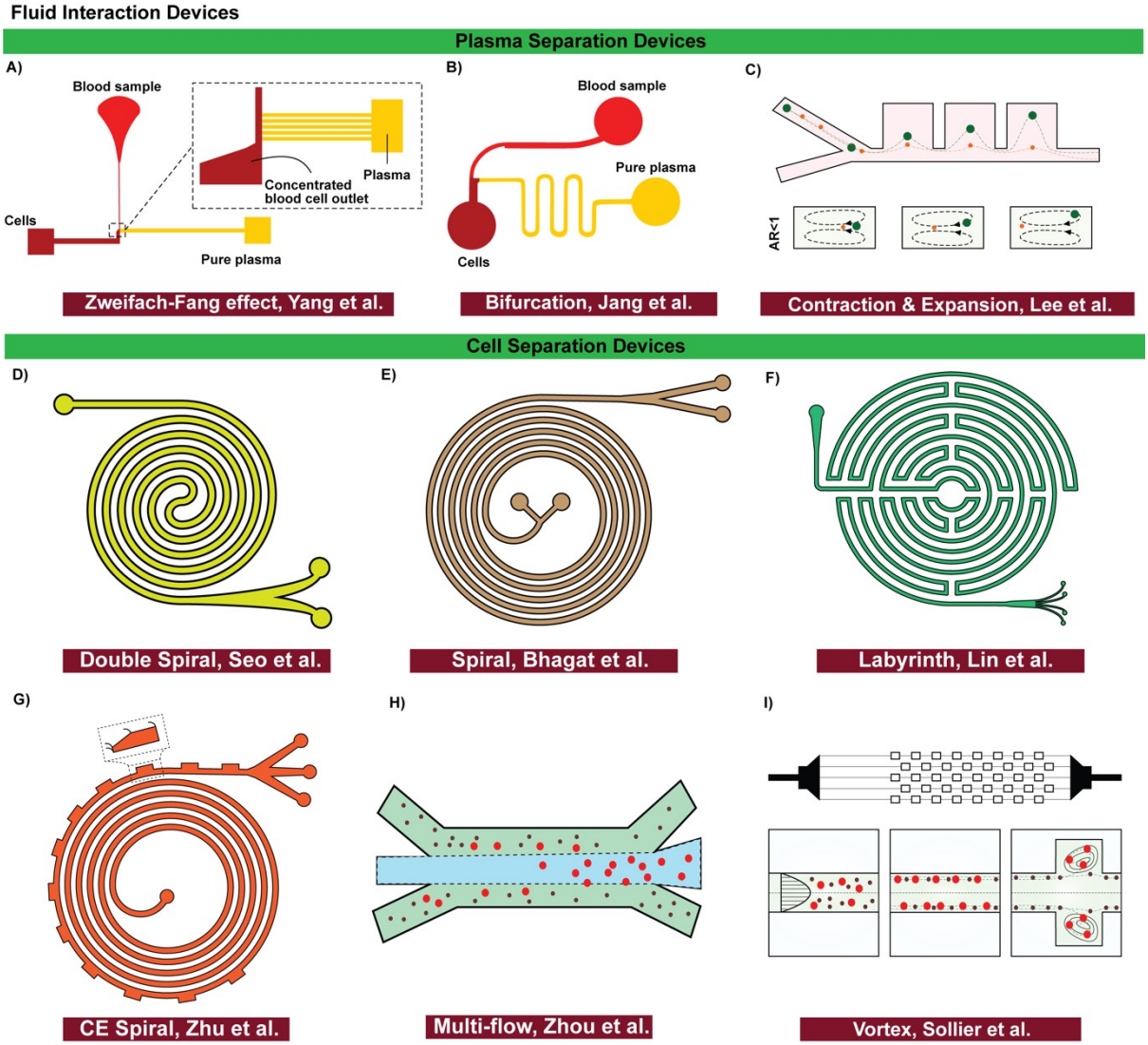
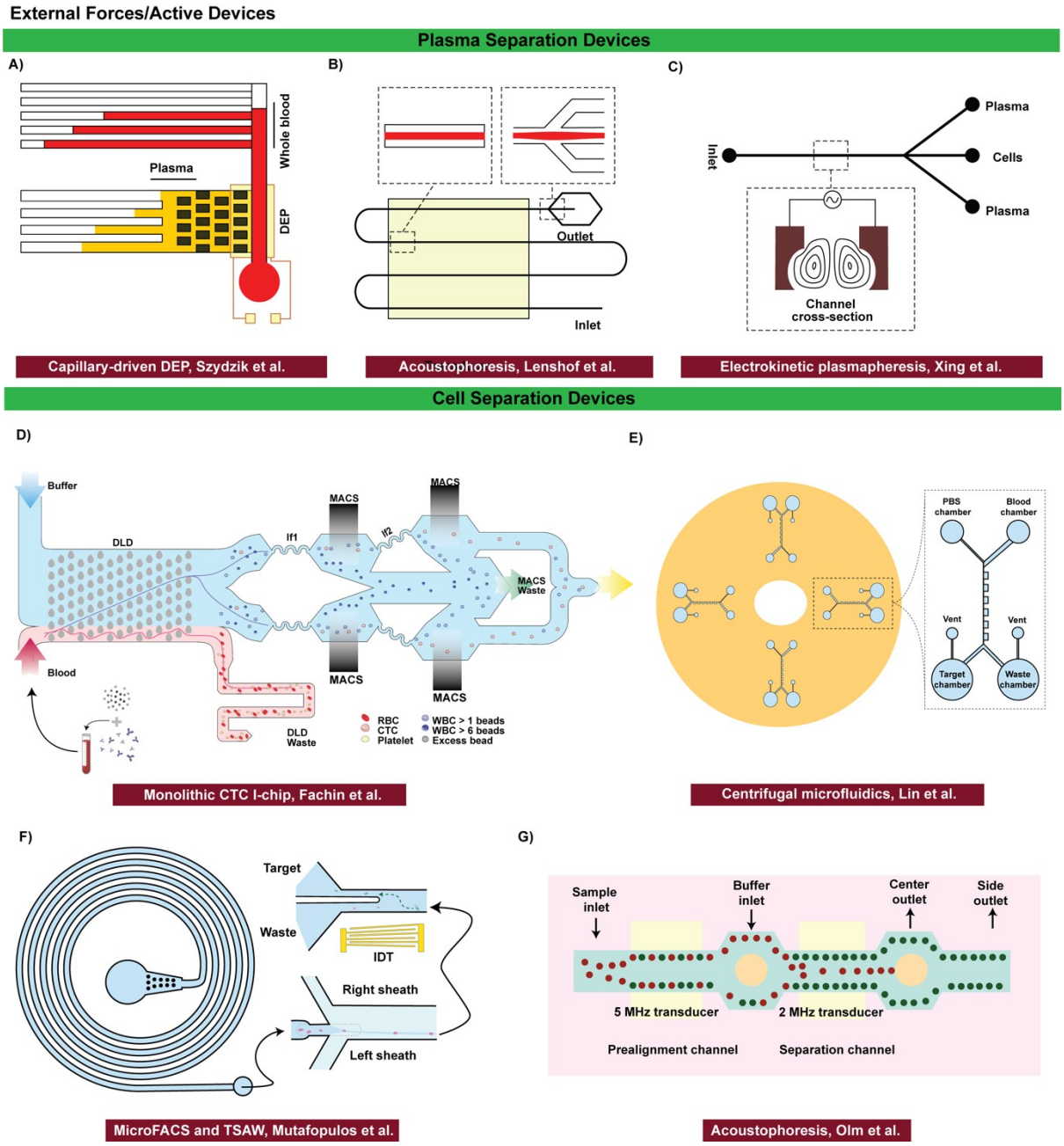
Supplements



Supplementary Figure 1 *Microfluidic devices that rely on solid interactions for blood fractionation.* ***Top Panel:*** *a selection of devices that rely on physical interactions to fractionate plasma,* ***A)*** *shows a simple device that uses beads to create a bead-packed region containing very small pores that will only allow plasma to pass through,* ***B)*** *also uses a bead-packed region to achieve filtration of plasma, in this case plasma filtration is achieved perpendicular to the fluid flow so that the plasma depleted blood can be further enriched for CTCs via RBC depletion and physical capture of CTCs in an array that will let smaller i.e. WBCs to pass but retain CTC's* ***C)*** *shows a DLD device that is especially tuned to produce plasma, to prevent blockage this is achieved in multiple phases.* ***Bottom panel:*** *devices for Physical enrichment of CTCs and CTC clusters.* ***D)*** *provides and overview and cross section of the Parsortix device which uses a stepped filtration mechanism to enrich for CTC via depletion of smaller cells, to reduce chance of blockage, filtration occurs perpendicular to the main direction of fluid flow,* ***E)*** *shows the Cross chip which uses parallel filtration arrays (arranged in a cross format) to achieve physical capture of CTCs via spacing of pillars to retard the motion of large cells.* ***F), G)*** *and* ***H)*** *depicts Affinity Capture devices, these are the Oncobean, GO Chip and Herringbone chips respectively. These chips all attempt to bring cell into contact with the surface of the chips so that antibody mediated binding can capture the cells to the walls of the device.* ***I) and J)*** *show devices that utilize physical interactions in a DLD array to enrich CTCs and CTC clusters. All the devices use a 2-stage filtration approach.* ***I)*** *shows a DLD array that is tuned to first enrich the large CTCs clusters in stage 1 and then proceed to capture smaller CTC cluster in stage 2.* ***J)*** *shows the NISA device and* ***K)*** *shows the CFD chip.*



Supplementary Figure 2 Microfluidic devices that utilize fluid interactions for blood fractionation. ***Top Panel:*** *a selection of devices that rely on fluid interactions to fractionate plasma,* ***A)*** *show a device that utilizes the Zweifach-Fang effect by skimming plasma using a series of small channels located perpendicular to the flow of blood.* ***B)*** *shows the overview of a bifurcation device where plasma can be skimmed where the microfluidic channel rapidly expands.* ***C)*** *provides an overview of the geometry and working principles of a Contraction and Expansion device where inertial forces effectively capture cells in expansion regions of channels and can thus provide cell depleted plasma.* ***Bottom panel:*** *devices that utilize fluid interactions to enrich CTCs. Top row shows 3 spiral devices which use a combination of Inertial lift forces and Dean drag forces to drive migration of large cells to the inner edge of the spiral channel and introduce channel bifurcation(s) to allow collection of different sized cells.* ***D)*** *shows the original spiral device (2008) which consists of the fusion of 2 spirals joined at the centre.* ***E)*** *shows the first single.* ***F)*** *shows a modified spiral device by Lin et.al.* ***G)*** *further modifies the spiral design by incorporating a series of expansion areas in the final loop of the outer spiral.* ***H)*** *moves away from the spiral design and utilizes the behaviour of particles in a straight channel while* ***I)*** *shows the vortex chip which operates under a similar principle to the Contraction and Expansion devices for plasma but is tuned to capture only large cells.*



Supplementary Figure 3. Microfluidic devices that utilise external forces or an active mechanism for blood fractionation. ***Top Panel:*** *devices for plasma isolation* ***A)*** *a capillary plasma enrichment device that uses dielectrophoresis (DEP) to keep the openings of the plasma channels for being clogged during operation.* ***B)*** *acoustophoretic device for separation of plasma for whole blood by sequentially removing focused blood cells at three separate point along the channel and* ***C)*** *a device by Xing et al. that utilises electrokinesis for separation of low volumes of plasma.* ***Bottom Panel:*** *device for CTC enrichment.* ***D)*** *the Monolithic CTC device from Fachin et.al uses all three approaches of solid interactions (DLD array), fluidic interaction (serpentine channels for inertial focusing) and external force (MACS) for CTC isolation from blood,* ***E)*** *a Lab-on-a disk device based off the contraction expansion channels in order to isolate cancer cells on the basis on size,* ***F)*** *microfluidic fluorescence activated cell-sorting (mFACS) device that combines a spiral device (inertial)to align and evenly distribute cells prior to analysing them and using traveling surface acoustic waves (TSAW) to effect gentle cell sorting, and* ***G)*** *device create by Olm et.al which used acoustophoresis for separating Neuroblastoma cells from blood.*