

# »» CELL POPULATION ARRAY IMAGER (CPAI)

ISIS PROJECT NUMBER 1547

## The Oxford invention

The CPAI is a specialised simple microscope which measures weak light signals over minutes to hours. The signals come from individual live cells introduced into it as a suspension, such as blood cells. Fluorescent or luminescent reporter molecules are pre-incorporated into the cells by well-established methods.

The heart of the CPAI is an imaging optical fibre-bundle forming a close-packed array of ultramicrowells imaged by a sensitive digital camera. Each well accommodates just one cell. Images of thousands of cells are acquired every few seconds.

The fibre-bundle is in a closed flow-chamber so that cells can react with substances micro-pumped through it in solution. Some of the cells may brighten transiently, with characteristic patterns. For instance T lymphocytes react to anti-receptor antibodies that stimulate calcium oscillations. For a few tens of minutes some of the cells wink like lighthouses, displaying a range of time-variant patterns. Proprietary neural-network-based pattern-recognition algorithms running on an ordinary laptop computer then automate the classification of the winks into characteristic cell subpopulations.

For the first time we can classify cells into subsets primarily according to their biochemical function, not by molecular marker.

This CPAI is an inexpensive and portable research instrument, in comparison with conventional flow cytometers or

fluorescence microscopes. It is likely to improve 'omic' strategies by screening large tethered arrays of protein or RNA ligands, and also has the potential to be developed as a field-portable cytometer with primary healthcare and third-world applications.

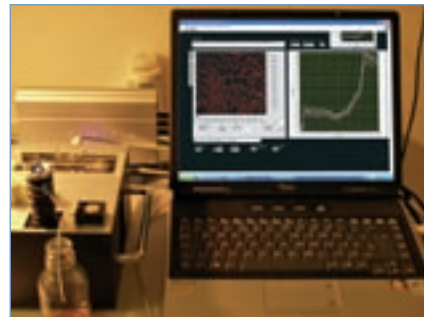
## Solutions provided by this invention

The CPAI solves all the limitations that afflict two related technologies:

1. Conventional video-imaging by fluorescence microscope to record signals from cell populations is constrained by:
  - › limited number of cells analysed, so subset-typical patterns are not identifiable
  - › cells being displaced by reagent passage during image acquisition, so data are lost
  - › cumbersome and expensive equipment
  - › requirement for relatively large cell numbers
2. Flow cytometers, when used for time-varying functional studies, assume each cell behaves identically to all the others in the sample. They measure only the average of the whole population; so individual differences are hidden.

## Potential applications

- › CPAI can be developed into a field-portable clinical diagnostic aid for any health diagnosis where altered patterns of cell signalling patterns following a suitable trigger would be revealing, for examples, blood



leukocyte/erythrocyte/semen/milk leukocyte/mouthwash testing.

- › Examples of possibilities after further R&D might include: malaria; polycystic kidney disease; autism; H5N1 flu infection; diseases with Th1/Th2 imbalances including arthritis and autoimmunity; immune status of transplant recipients; male infertility.
- › Scientific instrument opening up new strategies for fundamental research: CPAI is likely to reveal cell subpopulations not previously suspected.

## Patent status

This work is the subject of a patent application. Interested parties are welcome to discuss with Isis Innovation on how to utilise this invention.

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