

CLAIMS

1. A device for characterisation of one or more particles in a fluid sample, the device
5 comprising:
an inlet;
an outlet;
a microfluidic channel extending between the inlet and the outlet and providing an axial
flow path for fluid flowing therealong;
10 a particle sensor for detecting the passage of particles moving along the axial flow path
first and second electrodes positioned along the microfluidic channel; and
wherein, in use, one or more particles flowing along the microfluidic channel are
detected by the first particle sensor and passage of said one or more particles is
recorded as a pulse (e.g. a resistive pulse).
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2. A device according to Claim 1, wherein the particle sensor is located within the
microfluidic channel or extends at an angle to the microfluidic channel.
3. A device for characterisation of one or more particles in a fluid sample, the device
20 comprising:
a first particle sensor comprising a base comprising a microfluidic channel, wherein the
microfluidic channel comprises a first electrode and a second electrode positioned
along the microfluidic channel, and a detection region between the first and second
electrodes;
25 an inlet; and
an outlet,
wherein in use, a fluid sample comprising at least one particle flows in through the
inlet, along the microfluidic channel of the first particle sensor, over the first and
second electrodes, and exits through the fluid outlet, and wherein the passage of said
30 at least one particle through the detection region is recorded as a pulse (e.g. a
resistive pulse).
4. The device according to claim 1, 2 or 3, wherein the first particle sensor is configured
to detect particles of from 1 μm to 100 μm in size.
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5. The device according to any of claims 1 to 4, wherein the device further comprises at
least one second particle sensor.

6. The device according to Claim 5, wherein the second particle sensor extends at an angle to the microfluidic channel.
- 5 7. The device according to Claim 5 or 6, wherein the = second particle sensor provides a flow path for particles.
8. The device according to Claim 5, 6 or 7, wherein the second particle sensor or the flow path extends obtusely, acutely or orthogonal to the microfluidic channel or to the axial flow
10 path.
9. The device according to any of claims 5 to 8, wherein the second particle sensor is configured to detect particles within a different size range to the first particle sensor, for example to detect particles of from 1 nm to 1 μ m in size.
- 15 10. The device according to any of claims 5 to claim 9, wherein the second particle sensor is located downstream of the detection region of the first particle sensor
11. The device according to any of Claims 5 to 10, wherein the second particle sensor
20 comprises a nanopore.
12. The device according to any claim 11, wherein the nanopore of the second particle sensor is located in a second channel which extends from the microfluidic channel of the first particle sensor, optionally wherein the second channel extends perpendicularly from the
25 microfluidic channel.
13. The device according to any one of claims 11 to 12, wherein the nanopore of the second particle sensor is a solid state nanopore comprising a hole formed in a membrane.
- 30 14. The device according to claim 13, wherein the membrane is formed from a material selected from the group consisting of silicon nitride, silicon dioxide, polyurethane and polyester.
15. The device according to any one of claims 11 to 14, wherein the nanopore is provided
35 in a nanopipette.
16. The device according to any of Claims 5 to 15 wherein the second particle sensor comprises an electrode.

17. The device according to any one of claims 11 to 16, wherein the second particle sensor comprises a holder which houses the nanopore and an electrode, wherein the holder has a second channel therein in which the nanopore is located.

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18. The device according to claim 17, wherein the holder is in the form of a plug or screw which is releasably inserted into a port in the base of the first particle sensor, such that a fluid connection is formed between the microfluidic channel and the second channel.

10 19. The device according to any one of claims 5 to 18, wherein the second particle sensor comprises a tube in fluid communication with the second channel, wherein the tube provides a further fluid outlet.

15 20. The device according to any one of claims 5 to 19, comprising two or more second particle sensors.

21. The device according to claim 20, wherein each of the second particle sensors is configured to detect a different particle size range.

20 22. The device according to any one of claims 5 to 21, wherein the (or each) second particle sensor comprises, or is connected to, a flow regulator.

23. The device according to any preceding claim, wherein the device comprises a third sensor configured for measuring a parameter of the fluid, optionally wherein the parameter is selected from temperature, pH, oxygen content, ionic strength and viscosity.

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24. The device according to any preceding claim, wherein one or more of the components of the device are 3D printed, optionally wherein the base and/or the holder is 3D printed.

30 25. The device according to any preceding claim, wherein the device further comprises a lid which is configured to seal the microfluidic channel.

26. The device according to claim 25, wherein the lid comprises a primary ridge which is configured to be received within the microfluidic channel, thereby reducing the volume of the channel.

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27. The device according to claim 26, wherein the primary ridge further comprises a secondary ridge extending from the primary ridge, thereby creating a constriction within the channel.

5 28. The device according to claim 27, wherein the primary ridge and the secondary ridge together span the height and width of the microfluidic channel, and wherein the secondary ridge comprises a conduit which allows fluid to flow through the secondary ridge when the lid seals the microfluidic channel.

10 29. The device according to any one of claims 25 to 28, wherein the lid comprises a polymer layer on a surface of the lid which mates with the base so as to seal the microfluidic channel.

15 30. The device according to claim 29, wherein the polymer layer is a polydimethyl siloxane (PDMS).

31. The device according to any one of claims 25 to 30, wherein the lid is attached to the or a base with one or more screws.

20 32. The device according to claim 31 when dependent on claim 29 or claim 28, wherein upon tightening the screws the polymer layer can be forced into the microfluidic channel, thereby reducing the volume of the channel.

25 33. The device according to any preceding claim, wherein the base further comprises a groove which comprises an O-ring which surrounds the microfluidic channel and is configured to prevent leaks from the microfluidic channel.

34. The device according to any preceding claim, wherein the device is configured on a chip.

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35. A kit for characterisation of one or more particles in a fluid sample, the kit comprising:
- a device comprising a first particle sensor according to claim 1, 2 or 3; and
- at least one second particle sensor for connecting to the base of the first particle sensor, e.g. a second particle sensor according to any of claims 5 to 16.

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36. The kit according to claim 35, wherein the second particle sensor comprises a holder which houses a nanopore and an electrode, the holder having a second channel therein in

which the nanopore is located, and wherein the holder is configured to be releasably inserted into a port in the base of the first particle sensor.

37. The kit according to claim 35 or 36, wherein the kit comprises a plurality of second
5 particle sensors, wherein each of the second particle sensors comprises a nanopore having a diameter which is different to the diameter of a nanopore within each of the other second particle sensors.

38. The kit according to any one of claims 35 to 37, wherein the kit comprises at least one
10 third sensor for connecting to the base of the first particle sensor, wherein the third sensor is configured for measuring a parameter of the fluid selected from temperature, pH, oxygen content, ionic strength and viscosity.

39. A computer implemented method, comprising:
15 receiving, as an input from a particle sensor having first and second electrodes, pulse data representing a current pulse corresponding to a particle, and
comparing the received data to prestored characterising shape data representing particles of known shape;
determining, based on the comparison, a shape of the at least one particle; and
20 outputting an indication of the determined shape of the particle.

40. The method of claim 39, wherein the prestored characterising shape data comprises one or more spline coefficients representing the particles of known shape.

25 41. The method of claim 39, wherein the one or more spline coefficients are one or more spline coefficients for b-splines representing the particles of known shape.

42. The method of claim 39, wherein the one or more spline coefficients are a predetermined set of spline coefficients representing the particles of known shape.

30 43. The method of any of claims 39 to 42, wherein the prestored characterising shape data is for a normalised particle size, wherein the method comprises normalising the received pulse data.

44. The method of claim 39 wherein the prestored characterising shape data comprises an indication of a width of the current pulse.

45. The method of claim 39, wherein the prestored characterising shape data comprises
5 an indication of a maximal depth of the current pulse.

46. The method of any of claims 39 to 45, wherein the data representing the current pulse corresponding to the particle comprises pulse data corresponding to the particle traversing the sensor.

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47. The method of claim 46, wherein the pulse data representing the current pulse corresponding to the particle comprises pulse data corresponding to the particle traversing a nanopore.

15 48. The method of any of claims 39 to 47, the resistive pulse obtained by a device according to any of claims 1 to 34;

49. A computer implemented method, comprising:
receiving, as an input from a particle sensor having first and second electrodes, pulse
20 data representing a current pulse corresponding to a particle of known shape; and
determining a model in dependence on the received data indicative of the particle of known shape.

50. The method of claim 49, wherein the model is a classifier for classifying the pulse data
25 corresponding to the particle as one of a predetermined number of classes of particle shape.

51. The method of claim 49 or 50, comprising extracting the pulse data from raw pulse data comprising a plurality of pulses corresponding to a plurality of particles.

30 52. The method of any of claims 49 to 51, comprising normalising the pulse data to a predetermined magnitude.

53. The method of any of claims 49 to 52, wherein determining the model in dependence on the received data indicative of the particle of known shape comprises fitting the model to
35 the pulse data using a logistic regression method.

54. A computer-implemented method of characterising a nanoparticle, comprising:

receiving pulse data indicative of current flow between first and second electrodes associated with a microfluidic channel whilst the nanoparticle passes through the microfluidic channel;

- classifying the pulse data as corresponding to one of a plurality of predetermined types
5 of nanoparticle using a pulse-shape model.