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(71) Applicant *(for all designated States except US)*: **PURDUE RESEARCH FOUNDATION** [US/US]; 3000 Kent Avenue, West Lafayette, IN 47906 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **RAJWA, Bartlomiej, P.** [PL/US]; 543 Cumberland Avenue, West Lafayette, IN 47906 (US). **BERNAS, Tytus, S.** [PL/IE]; 21 Ridgeford Apts., Dundrum, Dublin, 14 (IE). **ROBINSON, Joseph, P.** [US/US]; 292 Park Lane, West Lafayette, IN 47906 (US).

(74) Agents: **GREENE, Nathan, O.** et al.; Brinks Hofer Gilson & Lione, P.O. Box 10087, Chicago, IL 60610 (US).

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[Continued on next page]

(54) Title: QUANTIFICATION OF DIFFERENCES BETWEEN MEASURED VALUES AND STATISTICAL VALIDATION BASED ON THE DIFFERENCES

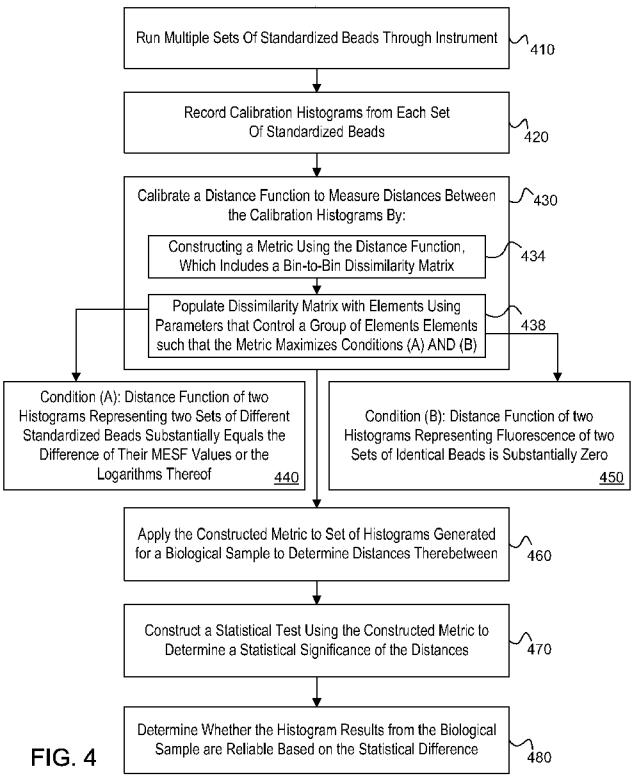

FIG. 4

(57) Abstract: A system and method of validating differences between measured values of fluorescence intensities obtained from a fluorescence-based instrument, including: generating calibration histograms for calibration beads run through the instrument; calibrating a distance function configured to measure distances between the histograms by: constructing a metric using the distance function, which includes a bin-to-bin dissimilarity matrix; and populating the dissimilarity matrix to maximize the following conditions: (A) the distance function of two histograms representing two sets of different beads equals the difference of their MESF values; and (B) the distance function of two histograms representing fluorescence of two sets of identical beads is zero; applying the metric to flow cytometry histograms generated for biological samples, to determine distances between the histograms; constructing a statistical test using the metric to determine a statistical significance of the distances; and determining whether the histogram results from the biological samples are reliable based on the statistical significance.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

C12Q 1/00(2006.01)i, G01N 33/50(2006.01)i, G06F 17/00(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 8: C12Q 1/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS, WPI, USPTO, PAJ "quantification, fluorescence, intensity, histogram, bin-to-bin dissimilarity matrix, quadratic form, molecules of equivalent soluble fluorophore value, etc."

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JONAS F. DORN et al. 'Computational processing and analysis of dynamic fluorescence image data.' In: Methods in Cell Biology. Available Online 22 December 2007, Vol. 85, pp.497-538. See the whole document.	1-28
A	JONATHAN W. COMEAU et al. 'A guide to accurate fluorescence microscopy colocalization measurements.' In: Biophysical Journal. December 2006, Vol.91(12), pp.4611-4622. See the whole document.	1-28
A	VOLODYMYR KUDRYAVTSEV et al. 'Monitoring dynamic systems with multiparameter fluorescence imaging.' In: Analytical and Bioanalytical Chemistry. Published Online 12 December 2006, Vol.387(1), pp.71-82. See the whole document.	1-28
A	SANTIAGO COSTANTINO et al. 'Accuracy and Dynamic range of spatial image correlation and cross-correlation spectroscopy.' In: Biophysical Journal. August 2005, Vol.89(2), pp.1251-1260. See the whole document.	1-28

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

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Name and mailing address of the ISA/KR
Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea
Facsimile No. 82-42-472-7140

Authorized officer
Heo, Joo-Hyung
Telephone No. 82-42-481-8150

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SANTIAGO COSTANTINO et al. 'Semi-automated quantification of filopodial dynamics.' In: Journal of Neuroscience Methods. Available Online 26. February 2008, Vol.171(1), pp.165-173. See the whole document.	1-28
P, X	TYTUS BERNAS et al. 'Quadratic form: a robust metric for quantitative comparison of flow cytometric histograms.' In: Cytometry Part A. Published Online 16 June 2008, Vol.73A(8), pp.715-726. See the whole document.	1-28