



(51) International Patent Classification:

G02B 21/36 (2006.01) G06T 7/33 (2017.01)

G05B 13/02 (2006.01) G06T 7/41 (2017.01)

G06T 7/00 (2017.01) G06T 7/77 (2017.01)

G06T 7/32 (2017.01)

(21) International Application Number:

PCT/US2018/037375

(22) International Filing Date:

13 June 2018 (13.06.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/518,975 13 June 2017 (13.06.2017) US

62/614,007 05 January 2018 (05.01.2018) US

(71) Applicant: **THE TRUSTEES OF PRINCETON UNIVERSITY** [US/US]; 87 Prospect Avenue, Princeton, NJ 08544 (US).

(72) Inventors: **SINGER, Amit**; c/o Princeton University, 87 Prospect Avenue, Princeton, NJ 08544 (US). **HEIMOWITZ, Ayelet**; c/o Princeton University, 87 Prospect Avenue, Princeton, NJ 08544 (US). **ANDEN, Joakim**; c/o Princeton University, 87 Prospect Avenue, Princeton, NJ 08544 (US). **KHOO, Yuehaw**; c/o Princeton University, 87 Prospect Avenue, Princeton, NJ 08544 (US). **KILEEL, Joseph**; c/o Princeton University, 87 Prospect Avenue, Princeton, NJ 08544 (US).

(74) Agent: **PAPROCKI, Andrew, J.** et al.; Michael Best & Friedrich LLP, 100 East Wisconsin Avenue, Suite 3300, Milwaukee, WI 53202-4108 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: FULLY AUTOMATIC, TEMPLATE -FREE PARTICLE PICKING FOR ELECTRON MICROSCOPY

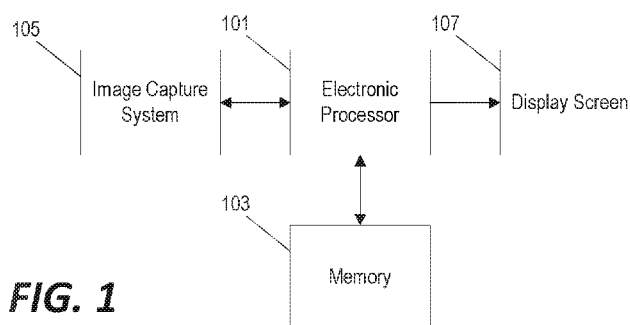


FIG. 1

(57) Abstract: Systems and methods are described for the fully automatic, template-free locating and extracting of a plurality of two-dimensional projections of particles in a micrograph image. A set of reference images is automatically assembled from a micrograph image by analyzing the image data in each of a plurality of partially overlapping windows and identifying a subset of windows with image data satisfying at least one statistic criterion compared to other windows. A normalized cross-correlation is then calculated between the image data in each reference image and the image data in each of a plurality of query image windows. Based on this cross-correlation analysis, a plurality of locations in the micrograph is automatically identified as containing a two-dimensional projection of a different instance of the particle of the first type. The two-dimensional projections identified in the micrograph are then used to determine the three-dimensional structure of the particle.



(88) Date of publication of the international search report:
19 December 2019 (19.12.2019)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 18/37375

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G02B 21/36, G05B 13/02, G06T 7/00, G06T 7/32, G06T 7/33, G06T 7/41, G06T 7/77 (2019.01)
 CPC - G02B 7/36, G02B 21/008, G02B 21/36, G02B 21/367, G05B 13/0265, G05B 23/0251, G05B 23/0281, G05B 23/0297, G05B 2219/35329, G05B 2219/39095, G05B 2219/40529, G05B 2219/42222, G05B 2219/45182, G06T 7/0014, G06T 7/32, G06T 7/337, G06T 7/41, G06T 7/44, G06T 7/49, G06T 7/77, G06T 2207/10056, G06T 2207/20004, G06T 2207/20012, G06T 2207/20016, G06T 2207/20021, G06T 2207/20024, G06T 2210/56

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)

See Search History Document

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

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2017-067746 A (NAKAMURA SANGYO GAKUEN, INST. INC. et al.) 06 April 2017 (06.04.2017), para [0011], [0030], [0141]	1-18
A	US 2009/0226096 A1 (NAMAI et al.) 10 September 2009 (10.09.2009), para [0010], [0040], [0043], [0090], [0092]	1-18
A	US 2008/0212880 A1 (HOMMAN et al.) 04 September 2008 (04.09.2008), para [0003], [0019], [0027], [0036], [0037]	1-18
A	US 7,418,693 B1 (GENNARI et al.) 26 August 2008 (26.08.2008), col 3, ln 51-67; col 4, ln 5-24; col 4, ln 55-65; col 10, ln 55 to col 11, ln 2	1-18
A	WO 03/105675 A2 (LIFESPAN BIOSCIENCES, INC.) 24 December 2003 (24.12.2003), pg 2, ln 12-26; col 31, ln 4-11; pg 46, ln 14-35	1-18

☐ 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

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"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

Date of the actual completion of the international search

30 September 2019

Date of mailing of the international search report

01 NOV 2019

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
 P.O. Box 1450, Alexandria, Virginia 22313-1450
 Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
 PCT OSP: 571-272-7774