(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 August 2009 (13.08.2009)

PCT

(10) International Publication Number
WO 2009/098596 A3

(51) International Patent Classification:
G06F 19/00 (2006.01) *C12N 15/11* (2006.01)
C12N 15/00 (2006.01) *C07K 14/00* (2006.01)
C40B 30/02 (2006.01) *G01N 33/68* (2006.01)

(21) International Application Number:
PCT/IB2009/005040

(22) International Filing Date:
5 February 2009 (05.02.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/026,435 5 February 2008 (05.02.2008) US
61/116,267 19 November 2008 (19.11.2008) US

(71) Applicant *(for all designated States except US)*: **ZYMEWORKS INC.**; 540-1385 West 8th Avenue, Vancouver, British Colombia V6H 3V9, (CA).

(71) Applicants and
(72) Inventors *(for all designated States except US)*: **LARIO, Paula, I.** [CA/CA]; 201-2080 E. Kent South, Vancouver, British Colombia V59 4X2 (CA). **MULLEGGER, Johannes** [AT/CA]; Suite 2 - 2135 Guelph Street, Vancouver, British Colombia V5T 3N7 (CA). **DIXIT, Surjit, B.** [IN/CA]; 5819 Dunbar Street, Vancouver, British Colombia V62 1W8 (CA). **RODINGER, Tomas** [CA/CA]; Apt 305-431 Pacific Street, Vancouver, British Colombia V6Z 2P5 (CA). **TAN, Powell, Patrick, Cheng** [CA/CA]; 11121 135A Street, Vancouver, British Colombia V3R 3A6 (CA).

(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, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

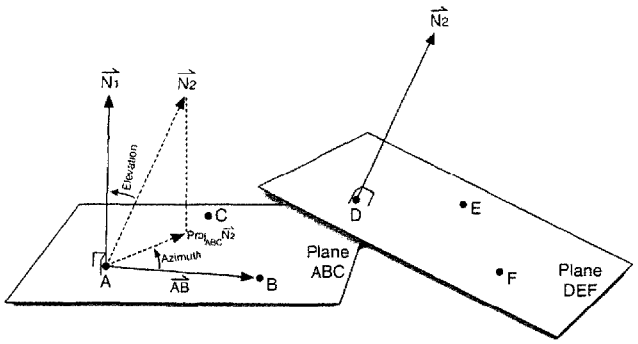
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,

[Continued on next page]

(54) Title: METHODS FOR DETERMINING CORRELATED RESIDUES IN A PROTEIN OR OTHER BIOPOLYMER USING MOLECULAR DYNAMICS

FIG. 1

Definition of "elevation" and "azimuth" angles between two planes



Definitions:
Plane ABC passes through atoms A, B, and C.
Plane DEF passes through atoms D, E, and F.
Vector N1 is normal to plane ABC.
Vector N2 is normal to plane DEF.
Vector AB is the vector pointing from atom A to atom B.
Elevation is the angle between vectors N1 and N2.
Azimuth is the angle between the projection of vector N2 onto plane ABC and vector AB.

(57) Abstract: The invention provides methods and systems of determining biopolymer profiles and correlations between structural units (residues) of a biopolymer based on sampling of the conformational space available to the molecule. The correlations between these structural units can further be used to find networks within a biopolymer such as the coupled residue networks in a protein. The invention also provides for designing and engineering biopolymers including polypeptides, nucleic acids and carbohydrates using the information derived from the conformation clustering and subsequent methods described herein.

WO 2009/098596 A3

MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, 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))*

(88) Date of publication of the international search report:
1 October 2009

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2009/005040

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***G06F 19/00*** (2006.01) , ***C12N 15/00*** (2006.01) , ***C40B 30/02*** (2006.01) , *C12N 15/11* (2006.01) , *C07K 14/00* (2006.01) , *G01N 33/68* (2006.01)
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)
G06F 19/00 (2006.01), *C12N 15/00* (2006.01), *C40B 30/02* (2006.01), *C12N 15/11* (2006.01), *C07K 14/00* (2006.01), *G01N 33/68* (2006.01)

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

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
WEST, Epoque, Pubmed, and Google Scholar

Keywords used: molecular, dynamics, simulation, model, monte carlo, plane, angle, rigid, mobile, flexible, peptide, structure, residue, side

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Fitzgerald et al, "Polypeptide Motions Are Dominated by Peptide Group Oscillations Resulting from Dihedral Angle Correlations between Nearest Neighbors", Biochemistry 2007, 46, pages 669-682 see the abstract and page 673, *Description of Observed Motions in Ala*$_7$	35
X	US 6 014 449 (Jacobs et al.) 11 January 2000 (11-01-2000) see column 5, line 64 - column 6, line 18	36 and 37
A	US 2003/0216867 A1 (Campbell et al.) 20 November 2003 (20-11-2003) see whole document	1-38
A	Kandiraju et al, "Dihedral Angle based Dimensionality Reduction for Protein Structural Comparison" Proceedings of the International Conference on Information Technology: Coding and Computing (ITCC'05) - Volume 1, pages 14-19, 4-6 April 2005 see whole document	1-38

[ ] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
17 July 2009 (17-07-2009)	30 July 2009 (30-07-2009)

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Kristina Bodnar 819- 934-5146

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Kishan et al., "Structural Biology, Protein Conformations and Drug Designing" Current Protein and Peptide Science, 2007, 8, 376-380 see the whole document	1-38

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2009/005040

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US 6014449A	11-01-2000	WO 9942951A1	26-08-1999
US 2003216867A1	20-11-2003	AU 2003220559A1	13-10-2003
		AU 2003220559A8	13-10-2003
		WO 03083438A2	09-10-2003
		WO 03083438A3	08-01-2004

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2009/005040

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 25
because they relate to subject matter not required to be searched by this Authority, namely :

Claim 25 outlines a method of medical treatment which is considered excluded subject matter.

2. [ ] Claim Nos. :
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.