Title (en)

METHOD AND COMPUTER PROGRAM PRODUCT FOR DRUG DISCOVERY USING WEIGHTED GRAND CANONICAL METROPOLIS MONTE CARLO SAMPLING

Title (de)

VERFAHREN UND COMPUTERPROGRAMMPRODUKT ZUM ENTDECKEN VON DROGEN DURCH VERWENDUNG GEWICHTETER GROSSER KANONISCHER METROPOLIS-MONTE-CARLO-STICHPROBEN

Title (fr)

PROCEDE ET PROGRAMME INFORMATIQUE PERMETTANT DE DECOUVRIR DES MEDICAMENTS A L'AIDE D'UN ECHANTILLONNAGE DE METROPOLIS MONTE CARLO GRAND-CANONIQUE PONDERE

Publication

EP 1644860 A4 20080806 (EN)

Application

EP 04776948 A 20040625

Priority

- US 2004020059 W 20040625
- US 48277403 P 20030627
- US 50927203 P 20031008
- US 50954303 P 20031009
- US 53168703 P 20031223
- US 74870803 A 20031231
- US 79418104 A 20040308

Abstract (en)

[origin: WO2005001645A2] A method and computer program product for modeling a system that includes a protein and a plurality of different fragment types in order to identify drug leads is presented. The basis of the method is a weighted Metropolis Monte Carlo approach for sampling the grand canonical ensemble. This method distinguishes itself from an energy minimization approach in that it provides fragment distributions which are consistent with thermal fluctuations at physiologically relevant temperatures. The weighted Metropolis Monte Carlo scheme performs a quasi-uniform sampling of all regions of interest on the protein, and, in this way, enables to resolve the wide range in densities of the thermodynamic distribution which could not be achieved by a non-weighted Metropolis scheme. Making use of the properties of the grand canonical ensemble, the affinity of fragments for different regions on the protein surface can be efficiently computed, using a so-called "simulated annealing of the chemical potential" process. A protein binding site is then identified as a region with high affinity for multiple fragments with a diverse set of physico-chemical properties. Within a binding site, assembly of fragments into drug leads is finally carried out based on binding affinity of the different fragments, on geometric proximity, and a variety of rules by which organic fragments may bond together.

IPC 8 full level

G16B 15/30 (2019.01); **G06G 7/48** (2006.01); **G06G 7/58** (2006.01)

IPC 8 main group level

G06F (2006.01)

CPC (source: EP US)

G16B 15/00 (2019.01 - EP); **G16B 15/30** (2019.01 - EP US); **G16C 20/50** (2019.01 - EP); G16C 10/00 (2019.01 - EP)

Citation (search report)

- [DX] GUARNIERI F ET AL: "SIMULATED ANNEALING OF CHEMICAL POTENTIAL: A GENERAL PROCEDURE FOR LOCATING BOUND WATERS. APPLICATION TO THE STUDY OF THE DIFFERENTIAL HYDRATION PROPENSITIES FOR THE MAJOR AND MINOR GROOVES OF DNA", JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, US, vol. 118, no. 35, 1 January 1996 (1996-01-01), pages 8493/8494, XP009061246, ISSN: 0002-7863
- [DX] CAFLISCH A ET AL: "Multiple copy simultaneous search and construction of ligands in binding sites: application to inhibitors of HIV-1 aspartic proteinase.", JOURNAL OF MEDICINAL CHEMISTRY 23 JUL 1993, vol. 36, no. 15, 23 July 1993 (1993-07-23), pages 2142 - 2167, XP002485505, ISSN: 0022-2623
- See references of WO 2005001645A2

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