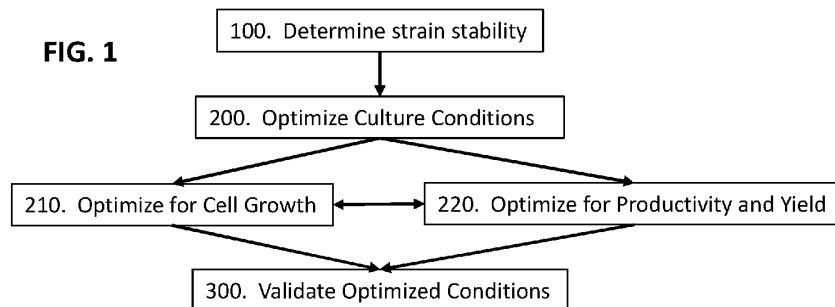




- (51) **International Patent Classification:**
G16B 20/00 (2019.01) *C12N 5/07* (2010.01)
- (21) **International Application Number:**
PCT/US2022/053733
- (22) **International Filing Date:**
21 December 2022 (21.12.2022)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/292,397 21 December 2021 (21.12.2021) US
- (71) **Applicant: POW GENETIC SOLUTIONS, INC.**
[US/US]; 2865 Seventh St., Berkeley, California 94710 (US).
- (72) **Inventors: HALL, Shannon;** 2865 Seventh St., Berkeley, California 94710 (US). **WANG, Ouwei;** 2865 Seventh St., Berkeley, California 94710 (US). **LEE, Brian;** 2865 Seventh St., Berkeley, California 94710 (US). **EMRICH, Charles;** 2865 Seventh St., Berkeley, California 94710 (US).
- (74) **Agent: STORELLA, John et al.;** Storella & Witt, LLP, 2625 Alcatraz Ave. #197, Berkeley, California 94705 (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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.
- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,

(54) **Title:** METHODS AND SYSTEMS FOR OPTIMIZING CULTURE CONDITIONS IN A CULTURE PROCESS

FIG. 1



(57) **Abstract:** Provided herein are methods and systems for iteratively improving culture condition for at least one culture output in a culture process. The methods comprise: a) providing a continuous culture of cells in a bioreactor, wherein the cells are cultured under culture conditions that comprise a set of culture parameters, and wherein the culture of cells produces at least one culture output at a first measure; b) while maintaining the cells in continuous culture, iteratively testing different culture conditions by: (i) selecting a new culture condition comprising a new set of culture parameters; wherein the new culture condition is predicted to improve the measure of the culture output, and is selected based on one or more prior measures of the culture output; (ii) perturbing the cells with the new culture conditions; and (iii) determining a new measure of the culture output; wherein testing is iterated to produce a plurality of improvements in the measure of culture output. The iterative process can be performed by an automated agent that uses direct search methods or deep learning techniques, such as reinforcement learning, to quickly find improved culture conditions.

[Continued on next page]

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, ME, 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).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

Published:

- *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*