

The Ploc_Bal-Mgpos is a Powerful Artificial Intelligence Tool for Predicting the Subcellular Localization of Gram-Positive Bacterial Proteins According to Their Sequence Information Alone

Kuo-Chen Chou*

Gordon Life Science Institute, Boston, Massachusetts 02478, USA

Received: February 15, 2023; **Accepted:** February 16, 2023; **Published:** February 19, 2023

Citation: Kuo-Chen C (2023) The Ploc_Bal-Mgpos is a Powerful Artificial Intelligence Tool for Predicting the Subcellular Localization of Gram-Positive Bacterial Proteins According to Their Sequence Information Alone. *Clar J Infect Dis Ther* 04(01): 280–292.

Recently a very useful web-server, or AI (Artificial Intelligence) tool, has been established for predicting the subcellular localization of Gram-positive bacterial proteins purely according to their sequences information for the multi-label systems [1], in which a same protein may occur or travel between two or more locations and hence its ID (identification) needs two or more labels as well, namely the “multi-label mark” [2].

The AI tool is named as “pLoc_bal-mGpos”, where “bal” stands for that the AI tool has been treated by balancing out the training dataset [3–9], and “m” for that the AI tool bears the capacity to deal with the multi-label systems. Below, let us demonstrate how the AI tool is working.

Clicking the link at http://www.jci-bioinfo.cn/pLoc_bal-mGpos/, you will see the top page of the pLoc_bal-mGpos web-server prompted on your computer’s screen (**Figure 1**). Then, click the Example button and use the query protein sequences as the input. After clicking the Submit button, you will see **Figure 2** shown on the screen of your computer. The corresponding outcomes were detailed in [4]. You can see from there: nearly all the success rates achieved by the AI tool for the Gram-positive bacterial proteins in each of the 6 subcellular locations are within the range of 98–99%. Such a high prediction quality is far beyond the reach of any of its counterparts.

In addition to the advantages of high accuracy and easy to use, the AI tool has been constructed by strictly complying with the “Chou’s 5-steps rule” and hence possesses the following terrific merits as concurred by many investigators (see, e.g., [10–91] as well as three comprehensive review papers [2, 92, 93]): (1) crystal clear in logic development, (2) completely transparent in operation, (3) easily to repeat the reported results by other investigators, (4) with high potential in stimulating other sequence-analyzing methods, and (5) very convenient to be used by the majority of experimental scientists.

Besides, the approach [94–96] of PseAAC (Pseudo Amino Acid Composition) has also been used during the development of the AI tool. It is a very powerful approach for formulating the samples of proteins by catching their special features, as done by many investigators [97–222].

Moreover, the IHTS (Inserting Hypothetical Training Samples) treatment has also been utilized to balance out the training dataset [57, 60, 84].

For the wonderful and awesome roles of the “5-steps rule” in driving proteome, genome analyses and drug development, see a series of recent papers [2, 93, 223–233] where the rule and its wide applications have been very impressively presented from various aspects or at different angles.

pLoc_bal-mGpos: predict subcellular localization of Gram-positive proteins by balancing training dataset and general PseAAC
[| Read Me](#) | [Supporting information](#) | [Citation](#) |

Enter query sequences

Enter the sequences of query proteins in FASTA format ([Example](#)): the number of proteins is limited at **10** or less for each submission.

Or, upload a file for batch prediction

Enter your e-mail address and upload the batch input file ([Batch-example](#)). The predicted result will be sent to you by e-mail once completed; it usually takes 1 minute or so for each protein sequence

Upload file:

Your Email:

Figure 1. A semi screenshot for the top page of pLoc_bal-mGpos (Adapted from [4] with permission).

pLoc_bal-mGpos: predict subcellular localization of Gram-positive proteins by balancing training dataset and general PseAAC
[| Read Me](#) | [Supporting information](#) | [Citation](#) |

Enter query sequences

Enter the sequences of query proteins in FASTA format ([Example](#)): the number of proteins is limited at **10** or less for each submission.

Or, upload a file for batch prediction

Enter your e-mail address and upload the batch input file ([Batch-example](#)). The predicted result will be sent to you by e-mail once completed; it usually takes 1 minute or so for each protein sequence

Upload file:

Your Email:

Figure 2. A semi screenshot for the webpage obtained by following Step 3 of Section 3.5 (Adapted from [4] with permission).

References

- [1] K.C. Chou, H.B. Shen, Recent progresses in protein subcellular location prediction. *Analytical Biochemistry* 370 (2007) 1–16.
- [2] K.C. Chou, Advance in predicting subcellular localization of multi-label proteins and its implication for developing multi-target drugs. *Current Medicinal Chemistry* 26 (2019) 4918–4943.
- [3] X. Xiao, X. Cheng, G. Chen, Q. Mao, K.C. Chou, pLoc_bal-mVirus: Predict Subcellular Localization of Multi-Label Virus Proteins by Chou's General PseAAC and IHTS Treatment to Balance Training Dataset. *Med Chem* 15 (2019) 496–509.
- [4] X. Xiao, X. Cheng, G. Chen, Q. Mao, K.C. Chou, pLoc_bal-mGpos: predict subcellular localization of Gram-positive bacterial proteins by quasi-balancing training dataset and PseAAC. *Genomics* 111 (2019) 886–892.
- [5] K.C. Chou, X. Cheng, X. Xiao, pLoc_bal-mEuk: predict subcellular localization of eukaryotic proteins by general PseAAC and quasi-balancing training dataset. *Med Chem* 15 (2019) 472–485.
- [6] K.C. Chou, X. Cheng, X. Xiao, pLoc_bal-mHum: predict subcellular localization of human proteins by PseAAC and quasi-balancing training dataset *Genomics* 111 (2019) 1274–1282.
- [7] X. Cheng, W.Z. Lin, X. Xiao, K.C. Chou, pLoc_bal-mAnimal: predict subcellular localization of animal proteins by balancing training dataset and PseAAC. *Bioinformatics* 35 (2019) 398–406.
- [8] X. Cheng, X. Xiao, K.C. Chou, pLoc_bal-mPlant: predict subcellular localization of plant proteins by general PseAAC and balancing training dataset *Curr Pharm Des* 24 (2018) 4013–4022.
- [9] X. Cheng, X. Xiao, K.C. Chou, pLoc_bal-mGneg: predict subcellular localization of Gram-negative bacterial proteins by quasi-balancing training dataset and general PseAAC. *Journal of Theoretical Biology* 458 (2018) 92–102.
- [10] A.H. Butt, Y.D. Khan, Prediction of S-Sulfenylation Sites Using Statistical Moments Based Features via Chou's 5-Step Rule. *International Journal of Peptide Research and Therapeutics (IJPR)* <https://doi.org/10.1007/s10989-019-09931-2> (2018).
- [11] M. Awais, W. Hussain, Y.D. Khan, N. Rasool, S.A. Khan, K.C. Chou, iPhosH-PseAAC: Identify phosphohistidine sites in proteins by blending statistical moments and position relative features according to the Chou's 5-step rule and general pseudo amino acid composition. *IEEE/ACM Trans Comput Biol Bioinform* <https://doi.org/10.1109/TCBB.2019.2919025> or <https://www.ncbi.nlm.nih.gov/pubmed/31144645> (2019).
- [12] O. Barukab, Y.D. Khan, S.A. Khan, K.C. Chou, iSulfoTyr-PseAAC: Identify tyrosine sulfation sites by incorporating statistical moments via Chou's 5-steps rule and pseudo components *Current Genomics* <https://doi.org/10.2174/1389202920666190819091609> or <http://www.eurekaselect.com/174277/article> (2019).
- [13] A.H. Butt, Y.D. Khan, Prediction of S-Sulfenylation Sites Using Statistical Moments Based Features via Chou's 5-Step Rule. *International Journal of Peptide Research and Therapeutics (IJPR)* <https://doi.org/10.1007/s10989-019-09931-2> (2019).
- [14] Y. Chen, X. Fan, Use of Chou's 5-Steps Rule to Reveal Active Compound and Mechanism of Shuangshen Pingfei San on Idiopathic Pulmonary Fibrosis. *Current Molecular Medicine* <https://doi.org/10.2174/1566524019666191011160543> (2019).
- [15] X. Du, Y. Diao, H. Liu, S. Li, MsDBP: Exploring DNA-binding Proteins by Integrating Multi-scale Sequence Information via Chou's 5-steps Rule. *Journal of Proteome Research* 18 (2019) 3119–3132.
- [16] A. Ehsan, M.K. Mahmood, Y.D. Khan, O.M. Barukab, S.A. Khan, K.C. Chou, iHyd-PseAAC (EPSV): Identify hydroxylation sites in proteins by extracting enhanced position and sequence variant feature via Chou's 5-step rule and general pseudo amino acid composition. *Current Genomics* 20 (2019) 124–133.
- [17] W. Hussain, S.D. Khan, N. Rasool, S.A. Khan, K.C. Chou, SPalmitoylC-PseAAC: A sequence-based model developed via Chou's 5-steps rule and general PseAAC for identifying S-palmitoylation sites in proteins. *Anal Biochem* 568 (2019) 14–23.
- [18] W. Hussain, Y.D. Khan, N. Rasool, S.A. Khan, K.C. Chou, SPrenylC-PseAAC: A sequence-based model developed via Chou's 5-steps rule and general PseAAC for identifying S-prenylation sites in proteins. *J Theor Biol* 468 (2019) 1–11.
- [19] Z. Ju, S.Y. Wang, Prediction of lysine formylation sites using the composition of k-spaced amino acid pairs via Chou's 5-steps rule and general pseudo components. *Genomics* <https://doi.org/10.1016/j.ygeno.2019.05.027> or <https://www.ncbi.nlm.nih.gov/pubmed/31175975> (2019).
- [20] M. Kabir, S. Ahmad, M. Iqbal, M. Hayat, iNR-2L: A two-level sequence-based predictor developed via Chou's 5-steps rule and general PseAAC for identifying nuclear receptors and their families. *Genomics* <https://www.ncbi.nlm.nih.gov/pubmed/30779939> (2019).
- [21] Z.U. Khan, F. Ali, I.A. Khan, Y. Hussain, D. Pi, iRSpot-SPI: Deep learning-based recombination spots prediction by incorporating secondary sequence information coupled with physio-chemical properties via Chou's

- 5-step rule and pseudo components. *Chemometrics and Intelligent Laboratory Systems (CHEMOLAB)* 189 (2019) 169–180.
- [22] J. Lan, J. Liu, C. Liao, D.J. Merkle, Q. Han, J. Li, A Study for Therapeutic Treatment against Parkinson's Disease via Chou's 5-steps Rule. *Current Topics in Medicinal Chemistry* <https://doi.org/10.2174/1568026619666191019111528> or <http://www.eurekaselect.com/175887/article> (2019).
- [23] N.Q.K. Le, iN6-methylat (5-step): identifying DNA N(6)-methyladenine sites in rice genome using continuous bag of nucleobases via Chou's 5-step rule. *Mol Genet Genomics* 294 (2019) 1173–1182.
- [24] N.Q.K. Le, E.K.Y. Yapp, Q.T. Ho, N. Nagasundaram, Y.Y. Ou, H.Y. Yeh, iEnhancer-5Step: Identifying enhancers using hidden information of DNA sequences via Chou's 5-step rule and word embedding. *Anal Biochem* 571 (2019) 53–61.
- [25] N.Q.K. Le, E.K.Y. Yapp, Y.Y. Ou, H.Y. Yeh, iMotor-CNN: Identifying molecular functions of cytoskeleton motor proteins using 2D convolutional neural network via Chou's 5-step rule. *Anal Biochem* 575 (2019) 17–26.
- [26] R. Liang, J. Xie, C. Zhang, M. Zhang, H. Huang, H. Huo, X. Cao, B. Niu, Identifying Cancer Targets Based on Machine Learning Methods via Chou's 5-steps Rule and General Pseudo Components. *Current Topics in Medicinal Chemistry* <https://doi.org/10.2174/1568026619666191016155543> (2019).
- [27] Y. Liang, S. Zhang, Identifying DNase I hypersensitive sites using multi-features fusion and F-score features selection via Chou's 5-steps rule. *Biophys Chem* 253 (2019) 106227.
- [28] S.J. Malebary, M.S.U. Rehman, Y.D. Khan, iCrotoK-PseAAC: Identify lysine crotonylation sites by blending position relative statistical features according to the Chou's 5-step rule. *PLoS One* 14 (2019) e0223993.
- [29] I. Nazari, M. Tahir, H. Tayari, K.T. Chong, iN6-Methyl (5-step): Identifying RNA N6-methyladenosine sites using deep learning mode via Chou's 5-step rules and Chou's general PseKNC. *Chemometrics and Intelligent Laboratory Systems (CHEMOLAB)* <https://doi.org/10.1016/j.chemolab.2019.103811> (2019).
- [30] Q. Ning, Z. Ma, X. Zhao, dForml(KNN)-PseAAC: Detecting formylation sites from protein sequences using K-nearest neighbor algorithm via Chou's 5-step rule and pseudo components. *J Theor Biol* 470 (2019) 43–49.
- [31] Salman, M. Khan, N. Iqbal, T. Hussain, S. Afzal, K.C. Chou, A two-level computation model based on deep learning algorithm for identification of piRNA and their functions via Chou's 5-steps rule. *International Journal of Peptide Research and Therapeutics (IJPR)* <https://doi.org/10.1007/s10989-019-09887-3> (2019).
- [32] M. Tahir, H. Tayara, K.T. Chong, iDNA6mA (5-step rule): Identification of DNA N6-methyladenine sites in the rice genome by intelligent computational model via Chou's 5-step rule. *CHEMOLAB* 189 (2019) 96–101.
- [33] S. Vishnoi, P. Garg, P. Arora, Physicochemical n-Grams Tool: A tool for protein physicochemical descriptor generation via Chou's 5-steps rule. *Chem Biol Drug Des* <https://doi.org/10.1111/cbdd.13617> or <https://www.ncbi.nlm.nih.gov/pubmed/31483930> (2019).
- [34] A. Wiktorowicz, A. Wit, A. Dziewierz, L. Rzeszutko, D. Dudek, P. Kleczynski, Calcium Pattern Assessment in Patients with Severe Aortic Stenosis Via the Chou's 5-Steps Rule. *Current Pharmaceutical Design* <https://doi.org/10.2174/1381612825666190930101258> (2019).
- [35] L. Yang, Y. Lv, S. Wang, Q. Zhang, Y. Pan, D. Su, Q. Lu, Y. Zuo, Identifying FL11 subtype by characterizing tumor immune microenvironment in prostate adenocarcinoma via Chou's 5-steps rule. *Genomics* <https://doi.org/10.1016/j.ygeno.2019.08.021> (2019).
- [36] L. Yang, Y. Lv, S. Wang, Q. Zhang, Y. Pan, D. Su, Q. Lu, Y. Zuo, Identifying FL11 subtype by characterizing tumor immune microenvironment in prostate adenocarcinoma via Chou's 5-steps rule. *Genomics* (2019).
- [37] Y.D. Khan, N. Amin, W. Hussain, N. Rasool, S.A. Khan, K.C. Chou, iProtease-PseAAC(2L): A two-layer predictor for identifying proteases and their types using Chou's 5-step-rule and general PseAAC. *Anal Biochem* 588 (2020) 113477.
- [38] Y. Xu, J. Ding, L.Y. Wu, K.C. Chou, iSNO-PseAAC: Predict cysteine S-nitrosylation sites in proteins by incorporating position specific amino acid propensity into pseudo amino acid composition *PLoS ONE* 8 (2013) e55844.
- [39] Y. Xu, X.J. Shao, L.Y. Wu, N.Y. Deng, K.C. Chou, iSNO-AAPair: incorporating amino acid pairwise coupling into PseAAC for predicting cysteine S-nitrosylation sites in proteins. *PeerJ* 1 (2013) e171.
- [40] Y. Xu, X. Wen, X.J. Shao, N.Y. Deng, K.C. Chou, iHyd-PseAAC: Predicting hydroxyproline and hydroxylysine in proteins by incorporating dipeptide position-specific propensity into pseudo amino acid composition. *International Journal of Molecular Sciences (IJMS)* 15 (2014) 7594–7610.
- [41] Y. Xu, X. Wen, L.S. Wen, L.Y. Wu, N.Y. Deng, K.C. Chou, iNitro-Tyr: Prediction of nitrotyrosine sites in proteins with general pseudo amino acid composition. *PLoS ONE* 9 (2014) e105018.

- [42] Y. Xu, K.C. Chou, Recent progress in predicting posttranslational modification sites in proteins. *Curr Top Med Chem* 16 (2016) 591–603.
- [43] L.M. Liu, Y. Xu, K.C. Chou, iPGK-PseAAC: identify lysine phosphoglycylation sites in proteins by incorporating four different tiers of amino acid pairwise coupling information into the general PseAAC. *Med Chem* 13 (2017) 552–559.
- [44] Y. Xu, C. Li, K.C. Chou, iPreNy-PseAAC: identify C-terminal cysteine prenylation sites in proteins by incorporating two tiers of sequence couplings into PseAAC. *Med Chem* 13 (2017) 544–551.
- [45] L. Cai, C.L. Wan, L. He, S. Jong, K.C. Chou, Gestational influenza increases the risk of psychosis in adults. *Medicinal Chemistry* 11 (2015) 676–682.
- [46] J. Liu, J. Song, M.Y. Wang, L. He, L. Cai, K.C. Chou, Association of EGF rs4444903 and XPD rs13181 polymorphisms with cutaneous melanoma in Caucasians. *Medicinal Chemistry* 11 (2015) 551–559.
- [47] L. Cai, Y.H. Yang, L. He, K.C. Chou, Modulation of cytokine network in the comorbidity of schizophrenia and tuberculosis. *Curr Top Med Chem* 16 (2016) 655–665.
- [48] L. Cai, W. Yuan, Z. Zhang, L. He, K.C. Chou, In-depth comparison of somatic point mutation callers based on different tumor next-generation sequencing depth data. *Scientific Reports* 6 (2016) 36540.
- [49] Y. Zhu, Q.W. Cong, Y. Liu, C.L. Wan, T. Yu, G. He, L. He, L. Cai, K.C. Chou, Antithrombin is an importantly inhibitory role against blood clots. *Curr Top Med Chem* 16 (2016) 666–674.
- [50] Z.D. Zhang, K. Liang, K. Li, G.Q. Wang, K.W. Zhang, L. Cai, S.T. Zha, K.C. Chou, *Chlorella vulgaris* induces apoptosis of human non-small cell lung carcinoma (NSCLC) cells. *Med Chem* 13 (2017) 560–568.
- [51] L. Cai, T. Huang, J. Su, X. Zhang, W. Chen, F. Zhang, L. He, K.C. Chou, Implications of newly identified brain eQTL genes and their interactors in Schizophrenia. *Molecular Therapy - Nucleic Acids* 12 (2018) 433–442.
- [52] B. Niu, M. Zhang, P. Du, L. Jiang, R. Qin, Q. Su, F. Chen, D. Du, Y. Shu, K.C. Chou, Small molecular floribundiquinone B derived from medicinal plants inhibits acetylcholinesterase activity. *Oncotarget* 8 (2017) 57149–57162.
- [53] Q. Su, W. Lu, D. Du, F. Chen, B. Niu, K.C. Chou, Prediction of the aquatic toxicity of aromatic compounds to *tetrahymena pyriformis* through support vector regression. *Oncotarget* 8 (2017) 49359–49369.
- [54] Y. Lu, S. Wang, J. Wang, G. Zhou, Q. Zhang, X. Zhou, B. Niu, Q. Chen, K.C. Chou, An Epidemic Avian Influenza Prediction Model Based on Google Trends. *Letters in Organic Chemistry* 16 (2019) 303–310.
- [55] B. Niu, C. Liang, Y. Lu, M. Zhao, Q. Chen, Y. Zhang, L. Zheng, K.C. Chou, Glioma stages prediction based on machine learning algorithm combined with protein-protein interaction networks. *Genomics* doi: 10.1016/j.ygeno.2019.05.024Get (2019).
- [56] J. Jia, Z. Liu, X. Xiao, B. Liu, K.C. Chou, Identification of protein-protein binding sites by incorporating the physicochemical properties and stationary wavelet transforms into pseudo amino acid composition (iPPBS-PseAAC). *J Biomol Struct Dyn (JBSD)* 34 (2016) 1946–1961.
- [57] J. Jia, Z. Liu, X. Xiao, B. Liu, K.C. Chou, iSuc-PseOpt: Identifying lysine succinylation sites in proteins by incorporating sequence-coupling effects into pseudo components and optimizing imbalanced training dataset. *Anal Biochem* 497 (2016) 48–56.
- [58] J. Jia, Z. Liu, X. Xiao, B. Liu, K.C. Chou, pSuc-Lys: Predict lysine succinylation sites in proteins with PseAAC and ensemble random forest approach. *Journal of Theoretical Biology* 394 (2016) 223–230.
- [59] J. Jia, Z. Liu, X. Xiao, B. Liu, K.C. Chou, iCar-PseCp: identify carbonylation sites in proteins by Monto Carlo sampling and incorporating sequence coupled effects into general PseAAC. *Oncotarget* 7 (2016) 34558–34570.
- [60] J. Jia, Z. Liu, X. Xiao, B. Liu, K.C. Chou, iPPBS-Opt: A Sequence-Based Ensemble Classifier for Identifying Protein-Protein Binding Sites by Optimizing Imbalanced Training Datasets. *Molecules* 21 (2016) E95.
- [61] J. Jia, L. Zhang, Z. Liu, X. Xiao, K.C. Chou, pSumo-CD: Predicting sumoylation sites in proteins with covariance discriminant algorithm by incorporating sequence-coupled effects into general PseAAC. *Bioinformatics* 32 (2016) 3133–3141.
- [62] Z. Liu, X. Xiao, D.J. Yu, J. Jia, W.R. Qiu, K.C. Chou, pRNAm-PC: Predicting N-methyladenosine sites in RNA sequences via physical-chemical properties. *Anal Biochem* 497 (2016) 60–67.
- [63] X. Xiao, H.X. Ye, Z. Liu, J.H. Jia, K.C. Chou, iROSGPseKNC: predicting replication origin sites in DNA by incorporating dinucleotide position-specific propensity into general pseudo nucleotide composition. *Oncotarget* 7 (2016) 34180–34189.
- [64] W.R. Qiu, B.Q. Sun, X. Xiao, Z.C. Xu, J.H. Jia, K.C. Chou, iKcr-PseEns: Identify lysine crotonylation sites in histone proteins with pseudo components and ensemble classifier. *Genomics* 110 (2018) 239–246.
- [65] J. Jia, X. Li, W. Qiu, X. Xiao, K.C. Chou, iPPI-PseAAC(CGR): Identify protein-protein interactions by

- incorporating chaos game representation into PseAAC. *Journal of Theoretical Biology* 460 (2019) 195–203.
- [66] W. Chen, H. Ding, P. Feng, H. Lin, K.C. Chou, iACP: a sequence-based tool for identifying anticancer peptides. *Oncotarget* 7 (2016) 16895–16909.
- [67] W. Chen, P. Feng, H. Ding, H. Lin, K.C. Chou, Using deformation energy to analyze nucleosome positioning in genomes. *Genomics* 107 (2016) 69–75.
- [68] W. Chen, H. Tang, J. Ye, H. Lin, K.C. Chou, iRNA-PseU: Identifying RNA pseudouridine sites *Molecular Therapy - Nucleic Acids* 5 (2016) e332.
- [69] C.J. Zhang, H. Tang, W.C. Li, H. Lin, W. Chen, K.C. Chou, iOri-Human: identify human origin of replication by incorporating dinucleotide physicochemical properties into pseudo nucleotide composition. *Oncotarget* 7 (2016) 69783–69793.
- [70] W. Chen, P. Feng, H. Yang, H. Ding, H. Lin, K.C. Chou, iRNA-AI: identifying the adenosine to inosine editing sites in RNA sequences. *Oncotarget* 8 (2017) 4208–4217.
- [71] P. Feng, H. Ding, H. Yang, W. Chen, H. Lin, K.C. Chou, iRNA-PseColl: Identifying the occurrence sites of different RNA modifications by incorporating collective effects of nucleotides into PseKNC. *Molecular Therapy - Nucleic Acids* 7 (2017) 155–163.
- [72] W. Chen, H. Ding, X. Zhou, H. Lin, K.C. Chou, iRNA(m6A)-PseDNC: Identifying N6-methyladenosine sites using pseudo dinucleotide composition. *Analytical Biochemistry* 561–562 (2018) 59–65.
- [73] W. Chen, P. Feng, H. Yang, H. Ding, H. Lin, K.C. Chou, iRNA-3typeA: identifying 3-types of modification at RNA's adenosine sites. *Molecular Therapy: Nucleic Acid* 11 (2018) 468–474.
- [74] Z.D. Su, Y. Huang, Z.Y. Zhang, Y.W. Zhao, D. Wang, W. Chen, K.C. Chou, H. Lin, iLoc-lncRNA: predict the subcellular location of lncRNAs by incorporating octamer composition into general PseKNC. *Bioinformatics* 34 (2018) 4196–4204.
- [75] H. Yang, W.R. Qiu, G. Liu, F.B. Guo, W. Chen, K.C. Chou, H. Lin, iRSpot-Pse6NC: Identifying recombination spots in *Saccharomyces cerevisiae* by incorporating hexamer composition into general PseKNC *International Journal of Biological Sciences* 14 (2018) 883–891.
- [76] P. Feng, H. Yang, H. Ding, H. Lin, W. Chen, K.C. Chou, iDNA6mA-PseKNC: Identifying DNA N(6)-methyladenosine sites by incorporating nucleotide physicochemical properties into PseKNC. *Genomics* 111 (2019) 96–102.
- [77] Q.S. Du, S.Q. Wang, N.Z. Xie, Q.Y. Wang, R.B. Huang, K.C. Chou, 2L-PCA: A two-level principal component analyzer for quantitative drug design and its applications. *Oncotarget* 8 (2017) 70564–70578.
- [78] B. Liu, L. Fang, R. Long, X. Lan, K.C. Chou, iEnhancer-2L: a two-layer predictor for identifying enhancers and their strength by pseudo k-tuple nucleotide composition. *Bioinformatics* 32 (2016) 362–369.
- [79] B. Liu, R. Long, K.C. Chou, iDHS-EL: Identifying DNase I hypersensitive sites by fusing three different modes of pseudo nucleotide composition into an ensemble learning framework. *Bioinformatics* 32 (2016) 2411–2418.
- [80] B. Liu, S. Wang, R. Long, K.C. Chou, iRSpot-EL: identify recombination spots with an ensemble learning approach. *Bioinformatics* 33 (2017) 35–41.
- [81] B. Liu, F. Yang, K.C. Chou, 2L-piRNA: A two-layer ensemble classifier for identifying piwi-interacting RNAs and their function. *Molecular Therapy - Nucleic Acids* 7 (2017) 267–277.
- [82] B. Liu, K. Li, D.S. Huang, K.C. Chou, iEnhancer-EL: Identifying enhancers and their strength with ensemble learning approach. *Bioinformatics* 34 (2018) 3835–3842.
- [83] B. Liu, F. Weng, D.S. Huang, K.C. Chou, iRO-3wPseKNC: Identify DNA replication origins by three-window-based PseKNC. *Bioinformatics* 34 (2018) 3086–3093.
- [84] B. Liu, F. Yang, D.S. Huang, K.C. Chou, iPromoter-2L: a two-layer predictor for identifying promoters and their types by multi-window-based PseKNC. *Bioinformatics* 34 (2018) 33–40.
- [85] W.R. Qiu, B.Q. Sun, X. Xiao, Z.C. Xu, K.C. Chou, iHyd-PseCp: Identify hydroxyproline and hydroxylysine in proteins by incorporating sequence-coupled effects into general PseAAC. *Oncotarget* 7 (2016) 44310–44321.
- [86] W.R. Qiu, B.Q. Sun, X. Xiao, Z.C. Xu, K.C. Chou, iPTM-mLys: identifying multiple lysine PTM sites and their different types. *Bioinformatics* 32 (2016) 3116–3123.
- [87] W.R. Qiu, X. Xiao, Z.C. Xu, K.C. Chou, iPhos-PseEn: identifying phosphorylation sites in proteins by fusing different pseudo components into an ensemble classifier. *Oncotarget* 7 (2016) 51270–51283.
- [88] W.R. Qiu, S.Y. Jiang, B.Q. Sun, X. Xiao, X. Cheng, K.C. Chou, iRNA-2methyl: identify RNA 2'-O-methylation sites by incorporating sequence-coupled effects into general PseKNC and ensemble classifier. *Medicinal Chemistry* 13 (2017) 734–743.
- [89] W.R. Qiu, S.Y. Jiang, Z.C. Xu, X. Xiao, K.C. Chou, iRNAm5C-PseDNC: identifying RNA 5-methylcytosine sites by incorporating physical-chemical properties into

- pseudo dinucleotide composition. *Oncotarget* 8 (2017) 41178–41188.
- [90] W.R. Qiu, B.Q. Sun, X. Xiao, D. Xu, K.C. Chou, iPhos-PseEvo: Identifying human phosphorylated proteins by incorporating evolutionary information into general PseAAC via grey system theory. *Molecular Informatics* 36 (2017) UNSP 1600010.
- [91] X. Zhai, M. Chen, W. Lu, Accelerated search for perovskite materials with higher Curie temperature based on the machine learning methods. *Computational Materials Science* 151 (2018) 41–48.
- [92] K.C. Chou, Some remarks on protein attribute prediction and pseudo amino acid composition (50th Anniversary Year Review, 5-steps rule). *Journal of Theoretical Biology* 273 (2011) 236–247.
- [93] K.C. Chou, Impacts of pseudo amino acid components and 5-steps rule to proteomics and proteome analysis. *Current Topics in Medicinal Chemistry (CTMC)* (Special Issue ed. G.P. Zhou) <https://doi.org/10.2174/1568026619666191018100141> or <http://www.eurekaselect.com/175823/article> (2019).
- [94] K.C. Chou, Prediction of protein cellular attributes using pseudo amino acid composition. *PROTEINS: Structure, Function, and Genetics* (Erratum: *ibid.*, 2001, Vol.44, 60) 43 (2001) 246–255.
- [95] K.C. Chou, Using amphiphilic pseudo amino acid composition to predict enzyme subfamily classes. *Bioinformatics* 21 (2005) 10–19.
- [96] K.C. Chou, Pseudo amino acid composition and its applications in bioinformatics, proteomics and system biology. *Current Proteomics* 6 (2009) 262–274.
- [97] Y.S. Ding, T.L. Zhang, Using Chou's pseudo amino acid composition to predict subcellular localization of apoptosis proteins: an approach with immune genetic algorithm-based ensemble classifier. *Pattern Recognition Letters* 29 (2008) 1887–1892.
- [98] Y. Fang, Y. Guo, Y. Feng, M. Li, Predicting DNA-binding proteins: approached from Chou's pseudo amino acid composition and other specific sequence features. *Amino Acids* 34 (2008) 103–109.
- [99] X. Jiang, R. Wei, T.L. Zhang, Q. Gu, Using the concept of Chou's pseudo amino acid composition to predict apoptosis proteins subcellular location: an approach by approximate entropy. *Protein & Peptide Letters* 15 (2008) 392–396.
- [100] X. Jiang, R. Wei, Y. Zhao, T. Zhang, Using Chou's pseudo amino acid composition based on approximate entropy and an ensemble of AdaBoost classifiers to predict protein subnuclear location. *Amino Acids* 34 (2008) 669–675.
- [101] F.M. Li, Q.Z. Li, Predicting protein subcellular location using Chou's pseudo amino acid composition and improved hybrid approach. *Protein & Peptide Letters* 15 (2008) 612–616.
- [102] H. Lin, The modified Mahalanobis discriminant for predicting outer membrane proteins by using Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 252 (2008) 350–356.
- [103] H. Lin, H. Ding, F.B. Feng-Biao Guo, A.Y. Zhang, J. Huang, Predicting subcellular localization of mycobacterial proteins by using Chou's pseudo amino acid composition. *Protein & Peptide Letters* 15 (2008) 739–744.
- [104] L. Nanni, A. Lumini, Genetic programming for creating Chou's pseudo amino acid based features for submitochondria localization. *Amino Acids* 34 (2008) 653–660.
- [105] G.Y. Zhang, H.C. Li, J.Q. Gao, B.S. Fang, Predicting lipase types by improved Chou's pseudo amino acid composition. *Protein & Peptide Letters* 15 (2008) 1132–1137.
- [106] S.W. Zhang, W. Chen, F. Yang, Q. Pan, Using Chou's pseudo amino acid composition to predict protein quaternary structure: a sequence-segmented PseAAC approach. *Amino Acids* 35 (2008) 591–598.
- [107] S.W. Zhang, Y.L. Zhang, H.F. Yang, C.H. Zhao, Q. Pan, Using the concept of Chou's pseudo amino acid composition to predict protein subcellular localization: an approach by incorporating evolutionary information and von Neumann entropies. *Amino Acids* 34 (2008) 565–572.
- [108] C. Chen, L. Chen, X. Zou, P. Cai, Prediction of protein secondary structure content by using the concept of Chou's pseudo amino acid composition and support vector machine. *Protein & Peptide Letters* 16 (2009) 27–31.
- [109] D.N. Georgiou, T.E. Karakasidis, J.J. Nieto, A. Torres, Use of fuzzy clustering technique and matrices to classify amino acids and its impact to Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 257 (2009) 17–26.
- [110] Z.C. Li, X.B. Zhou, Z. Dai, X.Y. Zou, Prediction of protein structural classes by Chou's pseudo amino acid composition: approached using continuous wavelet transform and principal component analysis. *Amino Acids* 37 (2009) 415–425.
- [111] H. Lin, H. Wang, H. Ding, Y.L. Chen, Q.Z. Li, Prediction of Subcellular Localization of Apoptosis Protein Using Chou's Pseudo Amino Acid Composition. *Acta Biotheoretica* 57 (2009) 321–330.
- [112] J.D. Qiu, J.H. Huang, R.P. Liang, X.Q. Lu, Prediction of G-protein-coupled receptor classes based on the concept

- of Chou's pseudo amino acid composition: an approach from discrete wavelet transform. *Analytical Biochemistry* 390 (2009) 68–73.
- [113] Y.H. Zeng, Y.Z. Guo, R.Q. Xiao, L. Yang, L.Z. Yu, M.L. Li, Using the augmented Chou's pseudo amino acid composition for predicting protein submitochondria locations based on auto covariance approach. *Journal of Theoretical Biology* 259 (2009) 366–372.
- [114] M. Esmaeili, H. Mohabatkar, S. Mohsenzadeh, Using the concept of Chou's pseudo amino acid composition for risk type prediction of human papillomaviruses. *Journal of Theoretical Biology* 263 (2010) 203–209.
- [115] Q. Gu, Y.S. Ding, T.L. Zhang, Prediction of G-Protein-Coupled Receptor Classes in Low Homology Using Chou's Pseudo Amino Acid Composition with Approximate Entropy and Hydrophobicity Patterns. *Protein & Peptide Letters* 17 (2010) 559–567.
- [116] H. Mohabatkar, Prediction of cyclin proteins using Chou's pseudo amino acid composition. *Protein & Peptide Letters* 17 (2010) 1207–1214.
- [117] J.D. Qiu, J.H. Huang, S.P. Shi, R.P. Liang, Using the concept of Chou's pseudo amino acid composition to predict enzyme family classes: an approach with support vector machine based on discrete wavelet transform. *Protein & Peptide Letters* 17 (2010) 715–722.
- [118] S.S. Sahu, G. Panda, A novel feature representation method based on Chou's pseudo amino acid composition for protein structural class prediction. *Computational Biology and Chemistry* 34 (2010) 320–327.
- [119] L. Yu, Y. Guo, Y. Li, G. Li, M. Li, J. Luo, W. Xiong, W. Qin, SecretP: Identifying bacterial secreted proteins by fusing new features into Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 267 (2010) 1–6.
- [120] J. Guo, N. Rao, G. Liu, Y. Yang, G. Wang, Predicting protein folding rates using the concept of Chou's pseudo amino acid composition. *Journal of Computational Chemistry* 32 (2011) 1612–1617.
- [121] J. Lin, Y. Wang, Using a novel AdaBoost algorithm and Chou's pseudo amino acid composition for predicting protein subcellular localization. *Protein & Peptide Letters* 18 (2011) 1219–1225.
- [122] J. Lin, Y. Wang, X. Xu, A novel ensemble and composite approach for classifying proteins based on Chou's pseudo amino acid composition. *African Journal of Biotechnology* 10 (2011) 16963–16968.
- [123] H. Mohabatkar, M. Mohammad Beigi, A. Esmaeili, Prediction of GABA(A) receptor proteins using the concept of Chou's pseudo amino acid composition and support vector machine. *Journal of Theoretical Biology* 281 (2011) 18–23.
- [124] B.M. Mohammad, M. Behjati, H. Mohabatkar, Prediction of metalloproteinase family based on the concept of Chou's pseudo amino acid composition using a machine learning approach. *Journal of Structural and Functional Genomics* 12 (2011) 191–197.
- [125] J.D. Qiu, S.B. Suo, X.Y. Sun, S.P. Shi, R.P. Liang, OligoPred: A web-server for predicting homo-oligomeric proteins by incorporating discrete wavelet transform into Chou's pseudo amino acid composition. *Journal of Molecular Graphics & Modelling* 30 (2011) 129–134.
- [126] D. Zou, Z. He, J. He, Y. Xia, Supersecondary structure prediction using Chou's pseudo amino acid composition. *Journal of Computational Chemistry* 32 (2011) 271–278.
- [127] J.Z. Cao, W.Q. Liu, H. Gu, Predicting Viral Protein Subcellular Localization with Chou's Pseudo Amino Acid Composition and Imbalance-Weighted Multi-Label K-Nearest Neighbor Algorithm. *Protein and Peptide Letters* 19 (2012) 1163–1169.
- [128] C. Chen, Z.B. Shen, X.Y. Zou, Dual-Layer Wavelet SVM for Predicting Protein Structural Class Via the General Form of Chou's Pseudo Amino Acid Composition. *Protein & Peptide Letters* 19 (2012) 422–429.
- [129] P. Du, X. Wang, C. Xu, Y. Gao, PseAAC-Builder: A cross-platform stand-alone program for generating various special Chou's pseudo amino acid compositions. *Analytical Biochemistry* 425 (2012) 117–119.
- [130] G.L. Fan, Q.Z. Li, Predict mycobacterial proteins subcellular locations by incorporating pseudo-average chemical shift into the general form of Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 304 (2012) 88–95.
- [131] G.L. Fan, Q.Z. Li, Predicting protein submitochondria locations by combining different descriptors into the general form of Chou's pseudo amino acid composition. *Amino Acids* 43 (2012) 545–555.
- [132] M. Hayat, A. Khan, Discriminating Outer Membrane Proteins with Fuzzy K-Nearest Neighbor Algorithms Based on the General Form of Chou's PseAAC. *Protein & Peptide Letters* 19 (2012) 411–421.
- [133] L.Q. Li, Y. Zhang, L.Y. Zou, Y. Zhou, X.Q. Zheng, Prediction of Protein Subcellular Multi-Localization Based on the General form of Chou's Pseudo Amino Acid Composition. *Protein & Peptide Letters* 19 (2012) 375–387.
- [134] B. Liao, Q. Xiang, D. Li, Incorporating Secondary Features into the General form of Chou's PseAAC for Predicting Protein Structural Class. *Protein & Peptide Letters* 19 (2012) 1133–1138.
- [135] L. Liu, X.Z. Hu, X.X. Liu, Y. Wang, S.B. Li, Predicting Protein Fold Types by the General Form of Chou's

- Pseudo Amino Acid Composition: Approached from Optimal Feature Extractions. *Protein & Peptide Letters* 19 (2012) 439–449.
- [136] S. Mei, Multi-kernel transfer learning based on Chou's PseAAC formulation for protein submitochondria localization. *Journal of Theoretical Biology* 293 (2012) 121–130.
- [137] S. Mei, Predicting plant protein subcellular multi-localization by Chou's PseAAC formulation based multi-label homolog knowledge transfer learning. *Journal of Theoretical Biology* 310 (2012) 80–87.
- [138] L. Nanni, S. Brahnam, A. Lumini, Wavelet images and Chou's pseudo amino acid composition for protein classification. *Amino Acids* 43 (2012) 657–65.
- [139] L. Nanni, A. Lumini, D. Gupta, A. Garg, Identifying bacterial virulent proteins by fusing a set of classifiers based on variants of Chou's pseudo amino acid composition and on evolutionary information. *IEEE-ACM Transaction on Computational Biology and Bioinformatics* 9 (2012) 467–475.
- [140] X.H. Niu, X.H. Hu, F. Shi, J.B. Xia, Predicting Protein Solubility by the General Form of Chou's Pseudo Amino Acid Composition: Approached from Chaos Game Representation and Fractal Dimension. *Protein & Peptide Letters* 19 (2012) 940–948.
- [141] Y.F. Qin, C.H. Wang, X.Q. Yu, J. Zhu, T.G. Liu, X.Q. Zheng, Predicting Protein Structural Class by Incorporating Patterns of Over- Represented k-mers into the General form of Chou's PseAAC. *Protein & Peptide Letters* 19 (2012) 388–397.
- [142] L.Y. Ren, Y.S. Zhang, I. Gutman, Predicting the Classification of Transcription Factors by Incorporating their Binding Site Properties into a Novel Mode of Chou's Pseudo Amino Acid Composition. *Protein & Peptide Letters* 19 (2012) 1170–1176.
- [143] X.Y. Sun, S.P. Shi, J.D. Qiu, S.B. Suo, S.Y. Huang, R.P. Liang, Identifying protein quaternary structural attributes by incorporating physicochemical properties into the general form of Chou's PseAAC via discrete wavelet transform. *Molecular BioSystems* 8 (2012) 3178–3184.
- [144] X.W. Zhao, Z.Q. Ma, M.H. Yin, Predicting protein-protein interactions by combing various sequence-derived features into the general form of Chou's Pseudo amino acid composition. *Protein & Peptide Letters* 19 (2012) 492–500.
- [145] Zia-ur-Rehman, A. Khan, Identifying GPCRs and their Types with Chou's Pseudo Amino Acid Composition: An Approach from Multi-scale Energy Representation and Position Specific Scoring Matrix. *Protein & Peptide Letters* 19 (2012) 890–903.
- [146] D.S. Cao, Q.S. Xu, Y.Z. Liang, propy: a tool to generate various modes of Chou's PseAAC. *Bioinformatics* 29 (2013) 960–962.
- [147] T.H. Chang, L.C. Wu, T.Y. Lee, S.P. Chen, H.D. Huang, J.T. Horng, EuLoc: a web-server for accurately predict protein subcellular localization in eukaryotes by incorporating various features of sequence segments into the general form of Chou's PseAAC. *Journal of Computer-Aided Molecular Design* 27 (2013) 91–103.
- [148] Y.K. Chen, K.B. Li, Predicting membrane protein types by incorporating protein topology, domains, signal peptides, and physicochemical properties into the general form of Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 318 (2013) 1–12.
- [149] G.-L. Fan, Q.-Z. Li, Y.-C. Zuo, Predicting acidic and alkaline enzymes by incorporating the average chemical shift and gene ontology informations into the general form of Chou's PseAAC. *Process Biochemistry* 48 (2013) 1048–1053.
- [150] G.L. Fan, Q.Z. Li, Discriminating bioluminescent proteins by incorporating average chemical shift and evolutionary information into the general form of Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 334 (2013) 45–51.
- [151] D.N. Georgiou, T.E. Karakasidis, A.C. Megaritis, A short survey on genetic sequences, Chou's pseudo amino acid composition and its combination with fuzzy set theory. *The Open Bioinformatics Journal* 7 (2013) 41–48.
- [152] M.K. Gupta, R. Niyogi, M. Misra, An alignment-free method to find similarity among protein sequences via the general form of Chou's pseudo amino acid composition. *SAR QSAR Environ Res* 24 (2013) 597–609.
- [153] C. Huang, J. Yuan, Using radial basis function on the general form of Chou's pseudo amino acid composition and PSSM to predict subcellular locations of proteins with both single and multiple sites. *Biosystems* 113 (2013) 50–57.
- [154] C. Huang, J.Q. Yuan, A multilabel model based on Chou's pseudo amino acid composition for identifying membrane proteins with both single and multiple functional types. *J Membr Biol* 246 (2013) 327–34.
- [155] C. Huang, J.Q. Yuan, Predicting protein subchloroplast locations with both single and multiple sites via three different modes of Chou's pseudo amino acid compositions. *Journal of Theoretical Biology* 335 (2013) 205–12.
- [156] M. Khosravian, F.K. Faramarzi, M.M. Beigi, M. Behbahani, H. Mohabatkar, Predicting Antibacterial Peptides by the Concept of Chou's Pseudo amino Acid Composition and Machine Learning Methods. *Protein & Peptide Letters* 20 (2013) 180–186.

- [157] H. Lin, C. Ding, L.-F. Yuan, W. Chen, H. Ding, Z.-Q. Li, F.-B. Guo, J. Huang, N.-N. Rao, Predicting subchloroplast locations of proteins based on the general form of Chou's pseudo amino acid composition: Approached from optimal tripeptide composition. *International Journal of Biomethmatics* 6 (2013) 1350003.
- [158] B. Liu, X. Wang, Q. Zou, Q. Dong, Q. Chen, Protein remote homology detection by combining Chou's pseudo amino acid composition and profile-based protein representation. *Molecular Informatics* 32 (2013) 775–782.
- [159] H. Mohabatkar, M.M. Beigi, K. Abdolahi, S. Mohsenzadeh, Prediction of Allergenic Proteins by Means of the Concept of Chou's Pseudo Amino Acid Composition and a Machine Learning Approach. *Medicinal Chemistry* 9 (2013) 133–137.
- [160] E. Pacharawongsakda, T. Theeramunkong, Predict Subcellular Locations of Singleplex and Multiplex Proteins by Semi-Supervised Learning and Dimension-Reducing General Mode of Chou's PseAAC. *IEEE Transactions on Nanobioscience* 12 (2013) 311–320.
- [161] Y.F. Qin, L. Zheng, J. Huang, Locating apoptosis proteins by incorporating the signal peptide cleavage sites into the general form of Chou's Pseudo amino acid composition. *International Journal of Quantum Chemistry* 113 (2013) 1660–1667.
- [162] A.N. Sarangi, M. Lohani, R. Aggarwal, Prediction of Essential Proteins in Prokaryotes by Incorporating Various Physico-chemical Features into the General form of Chou's Pseudo Amino Acid Composition. *Protein Pept Lett* 20 (2013) 781–95.
- [163] S. Wan, M.W. Mak, S.Y. Kung, GOASVM: A subcellular location predictor by incorporating term-frequency gene ontology into the general form of Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 323 (2013) 40–48.
- [164] X. Wang, G.Z. Li, W.C. Lu, Virus-ECC-mPLOC: a multi-label predictor for predicting the subcellular localization of virus proteins with both single and multiple sites based on a general form of Chou's pseudo amino acid composition. *Protein & Peptide Letters* 20 (2013) 309–317.
- [165] N. Xiaohui, L. Nana, X. Jingbo, C. Dingyan, P. Yuehua, X. Yang, W. Weiquan, W. Dongming, W. Zengzhen, Using the concept of Chou's pseudo amino acid composition to predict protein solubility: An approach with entropies in information theory. *Journal of Theoretical Biology* 332 (2013) 211–217.
- [166] H.L. Xie, L. Fu, X.D. Nie, Using ensemble SVM to identify human GPCRs N-linked glycosylation sites based on the general form of Chou's PseAAC. *Protein Eng Des Sel* 26 (2013) 735–742.
- [167] P. Du, S. Gu, Y. Jiao, PseAAC-General: Fast building various modes of general form of Chou's pseudo amino acid composition for large-scale protein datasets. *International Journal of Molecular Sciences* 15 (2014) 3495–3506.
- [168] Z. Hajisharifi, M. Piryaiee, M. Mohammad Beigi, M. Behbahani, H. Mohabatkar, Predicting anticancer peptides with Chou's pseudo amino acid composition and investigating their mutagenicity via Ames test. *Journal of Theoretical Biology* 341 (2014) 34–40.
- [169] G.S. Han, Z.G. Yu, V. Anh, A two-stage SVM method to predict membrane protein types by incorporating amino acid classifications and physicochemical properties into a general form of Chou's PseAAC. *J Theor Biol* 344 (2014) 31–9.
- [170] C. Jia, X. Lin, Z. Wang, Prediction of Protein S-Nitrosylation Sites Based on Adapted Normal Distribution Bi-Profile Bayes and Chou's Pseudo Amino Acid Composition. *Int J Mol Sci* 15 (2014) 10410–23.
- [171] L. Kong, L. Zhang, J. Lv, Accurate prediction of protein structural classes by incorporating predicted secondary structure information into the general form of Chou's pseudo amino acid composition. *J Theor Biol* 344 (2014) 12–18.
- [172] L. Li, S. Yu, W. Xiao, Y. Li, M. Li, L. Huang, X. Zheng, S. Zhou, H. Yang, Prediction of bacterial protein subcellular localization by incorporating various features into Chou's PseAAC and a backward feature selection approach. *Biochimie* 104 (2014) 100–7.
- [173] L. Nanni, S. Brahnam, A. Lumini, Prediction of protein structure classes by incorporating different protein descriptors into general Chou's pseudo amino acid composition. *J Theor Biol* 360 (2014) 109–116.
- [174] J. Zhang, P. Sun, X. Zhao, Z. Ma, PECM: Prediction of extracellular matrix proteins using the concept of Chou's pseudo amino acid composition. *Journal of Theoretical Biology* 363 (2014) 412–418.
- [175] J. Zhang, X. Zhao, P. Sun, Z. Ma, PSNO: Predicting Cysteine S-Nitrosylation Sites by Incorporating Various Sequence-Derived Features into the General Form of Chou's PseAAC. *Int J Mol Sci* 15 (2014) 11204–19.
- [176] L. Zhang, X. Zhao, L. Kong, Predict protein structural class for low-similarity sequences by evolutionary difference information into the general form of Chou's pseudo amino acid composition. *J Theor Biol* 355 (2014) 105–10.
- [177] Y.C. Zuo, Y. Peng, L. Liu, W. Chen, L. Yang, G.L. Fan, Predicting peroxidase subcellular location by hybridizing different descriptors of Chou's pseudo amino acid patterns. *Anal Biochem* 458 (2014) 14–9.

- [178] F. Ali, M. Hayat, Classification of membrane protein types using Voting Feature Interval in combination with Chou's Pseudo Amino Acid Composition. *J Theor Biol* 384 (2015) 78–83.
- [179] G.L. Fan, X.Y. Zhang, Y.L. Liu, Y. Nang, H. Wang, DSPMP: Discriminating secretory proteins of malaria parasite by hybridizing different descriptors of Chou's pseudo amino acid patterns. *J Comput Chem* 36 (2015) 2317–27.
- [180] C. Huang, J.Q. Yuan, Simultaneously Identify Three Different Attributes of Proteins by Fusing their Three Different Modes of Chou's Pseudo Amino Acid Compositions. *Protein Pept Lett* 22 (2015) 547–56.
- [181] Z.U. Khan, M. Hayat, M.A. Khan, Discrimination of acidic and alkaline enzyme using Chou's pseudo amino acid composition in conjunction with probabilistic neural network model. *J Theor Biol* 365 (2015) 197–203.
- [182] R. Kumar, A. Srivastava, B. Kumari, M. Kumar, Prediction of beta-lactamase and its class by Chou's pseudo amino acid composition and support vector machine. *J Theor Biol* 365 (2015) 96–103.
- [183] B. Liu, J. Xu, S. Fan, R. Xu, J. Jiyun Zhou, X. Wang, PseDNA-Pro: DNA-binding protein identification by combining Chou's PseAAC and physicochemical distance transformation. *Molecular Informatics* 34 (2015) 8–17
- [184] M. Mandal, A. Mukhopadhyay, U. Maulik, Prediction of protein subcellular localization by incorporating multiobjective PSO-based feature subset selection into the general form of Chou's PseAAC. *Med Biol Eng Comput* 53 (2015) 331–44.
- [185] V. Sanchez, A.M. Peinado, J.L. Perez-Cordoba, A.M. Gomez, A new signal characterization and signal-based Chou's PseAAC representation of protein sequences. *J Bioinform Comput Biol* 13 (2015) 1550024.
- [186] X. Wang, W. Zhang, Q. Zhang, G.Z. Li, MultiP-SChlo: multi-label protein subchloroplast localization prediction with Chou's pseudo amino acid composition and a novel multi-label classifier. *Bioinformatics* 31 (2015) 2639–45.
- [187] Y.S. Jiao, P.F. Du, Prediction of Golgi-resident protein types using general form of Chou's pseudo amino acid compositions: Approaches with minimal redundancy maximal relevance feature selection. *J Theor Biol* 402 (2016) 38–44.
- [188] M. Kabir, M. Hayat, iRSpot-GAEnsC: identifying recombination spots via ensemble classifier and extending the concept of Chou's PseAAC to formulate DNA samples. *Molecular Genetics and Genomics* 291 (2016) 285–96.
- [189] M. Tahir, M. Hayat, iNuc-STNC: a sequence-based predictor for identification of nucleosome positioning in genomes by extending the concept of SAAC and Chou's PseAAC. *Mol Biosyst* 12 (2016) 2587–93.
- [190] H. Tang, W. Chen, H. Lin, Identification of immunoglobulins using Chou's pseudo amino acid composition with feature selection technique. *Mol Biosyst* 12 (2016) 1269–1275.
- [191] H.L. Zou, X. Xiao, Predicting the Functional Types of Singleplex and Multiplex Eukaryotic Membrane Proteins via Different Models of Chou's Pseudo Amino Acid Compositions. *J Membr Biol* 249 (2016) 23–9.
- [192] H. Huo, T. Li, S. Wang, Y. Lv, Y. Zuo, L. Yang, Prediction of presynaptic and postsynaptic neurotoxins by combining various Chou's pseudo components. *Sci Rep* 7 (2017) 5827.
- [193] Z. Ju, J.J. He, Prediction of lysine propionylation sites using biased SVM and incorporating four different sequence features into Chou's PseAAC. *J Mol Graph Model* 76 (2017) 356–363.
- [194] M. Rahimi, M.R. Bakhtiarizadeh, A. Mohammadi-Sangcheshmeh, Oogenesis_Pred: A sequence-based method for predicting oogenesis proteins by six different modes of Chou's pseudo amino acid composition. *J Theor Biol* 414 (2017) 128–136.
- [195] P. Tripathi, P.N. Pandey, A novel alignment-free method to classify protein folding types by combining spectral graph clustering with Chou's pseudo amino acid composition. *J Theor Biol* 424 (2017) 49–54.
- [196] B. Yu, S. Li, W.Y. Qiu, C. Chen, R.X. Chen, L. Wang, M.H. Wang, Y. Zhang, Accurate prediction of subcellular location of apoptosis proteins combining Chou's PseAAC and PsePSSM based on wavelet denoising. *Oncotarget* 8 (2017) 107640–107665.
- [197] B. Yu, L. Lou, S. Li, Y. Zhang, W. Qiu, X. Wu, M. Wang, B. Tian, Prediction of protein structural class for low-similarity sequences using Chou's pseudo amino acid composition and wavelet denoising. *J Mol Graph Model* 76 (2017) 260–273.
- [198] J. Ahmad, M. Hayat, MFSC: Multi-voting based Feature Selection for Classification of Golgi Proteins by Adopting the General form of Chou's PseAAC components. *J Theor Biol* 463 (2018) 99–109.
- [199] S. Akbar, M. Hayat, iMethyl-STTNC: Identification of N(6)-methyladenosine sites by extending the Idea of SAAC into Chou's PseAAC to formulate RNA sequences. *J Theor Biol* 455 (2018) 205–211.
- [200] M.A. Al Maruf, S. Shatabda, iRSpot-SF: Prediction of recombination hotspots by incorporating sequence based features into Chou's Pseudo components. *Genomics* doi:10.1016/j.ygeno.2018.06.003 (2018).
- [201] M. Arif, M. Hayat, Z. Jan, iMem-2LSAAC: A two-level model for discrimination of membrane proteins and their types by extending the notion of SAAC into Chou's

- pseudo amino acid composition. *J Theor Biol* 442 (2018) 11–21.
- [202] E. Contreras-Torres, Predicting structural classes of proteins by incorporating their global and local physicochemical and conformational properties into general Chou's PseAAC. *J Theor Biol* 454 (2018) 139–145.
- [203] X. Cui, Z. Yu, B. Yu, M. Wang, B. Tian, Q. Ma, UbiSitePred: A novel method for improving the accuracy of ubiquitination sites prediction by using LASSO to select the optimal Chou's pseudo components. *Chemometrics and Intelligent Laboratory Systems (CHEMOLAB)* doi:10.1016/j.chemolab.2018.11.012 (2018).
- [204] X. Fu, W. Zhu, B. Liso, L. Cai, L. Peng, J. Yang, Improved DNA-binding protein identification by incorporating evolutionary information into the Chou's PseAAC. *IEEE Access* 20 (2018) <https://doi.org/10.1109/ACCESS.2018.2876656>.
- [205] F. Javed, M. Hayat, Predicting subcellular localizations of multi-label proteins by incorporating the sequence features into Chou's PseAAC. *Genomics* <https://doi.org/10.1016/j.ygeno.2018.09.004> (2018).
- [206] J. Mei, J. Zhao, Prediction of HIV-1 and HIV-2 proteins by using Chou's pseudo amino acid compositions and different classifiers. *Sci Rep* 8 (2018) 2359.
- [207] M. Mousavizadegan, H. Mohabatkar, Computational prediction of antifungal peptides via Chou's PseAAC and SVM. *J Bioinform Comput Biol* (2018) 1850016.
- [208] W. Qiu, S. Li, X. Cui, Z. Yu, M. Wang, J. Du, Y. Peng, B. Yu, Predicting protein submitochondrial locations by incorporating the pseudo-position specific scoring matrix into the general Chou's pseudo-amino acid composition. *J Theor Biol* 450 (2018) 86–103.
- [209] L. Zhang, L. Kong, iRSpot-ADPM: Identify recombination spots by incorporating the associated dinucleotide product model into Chou's pseudo components. *J Theor Biol* 441 (2018) 1–8.
- [210] S. Zhang, Y. Liang, Predicting apoptosis protein subcellular localization by integrating auto-cross correlation and PSSM into Chou's PseAAC. *J Theor Biol* 457 (2018) 163–169.
- [211] S. Zhang, K. Yang, Y. Lei, K. Song, iRSpot-DTS: Predict recombination spots by incorporating the dinucleotide-based spare-cross covariance information into Chou's pseudo components. *Genomics* 11 (2018) 457–464.
- [212] W. Zhao, L. Wang, T.X. Zhang, Z.N. Zhao, P.F. Du, A brief review on software tools in generating Chou's pseudo-factor representations for all types of biological sequences. *Protein Pept Lett* 25 (2018) 822–829.
- [213] J. Ahmad, M. Hayat, MFSC: Multi-voting based feature selection for classification of Golgi proteins by adopting the general form of Chou's PseAAC components. *J Theor Biol* 463 (2019) 99–109.
- [214] M.A. Al Maruf, S. Shatabda, iRSpot-SF: Prediction of recombination hotspots by incorporating sequence based features into Chou's Pseudo components. *Genomics* 111 (2019) 966–972.
- [215] A.H. Butt, N. Rasool, Y.D. Khan, Prediction of antioxidant proteins by incorporating statistical moments based features into Chou's PseAAC. *Journal of Theoretical Biology* 473 (2019) 1–8.
- [216] F. Javed, M. Hayat, Predicting subcellular localization of multi-label proteins by incorporating the sequence features into Chou's PseAAC. *Genomics* 111 (2019) 1325–1332.
- [217] Y. Pan, S. Wang, Q. Zhang, Q. Lu, D. Su, Y. Zuo, L. Yang, Analysis and prediction of animal toxins by various Chou's pseudo components and reduced amino acid compositions. *J Theor Biol* 462 (2019) 221–229.
- [218] M. Tahir, M. Hayat, S.A. Khan, iNuc-ext-PseTNC: an efficient ensemble model for identification of nucleosome positioning by extending the concept of Chou's PseAAC to pseudo-tri-nucleotide composition. *Mol Genet Genomics* 294 (2019) 199–210.
- [219] M. Tahir, H. Tayara, K.T. Chong, iRNA-PseKNC(2methyl): Identify RNA 2'-O-methylation sites by convolution neural network and Chou's pseudo components. *J Theor Biol* 465 (2019) 1–6.
- [220] B. Tian, X. Wu, C. Chen, W. Qiu, Q. Ma, B. Yu, Predicting protein-protein interactions by fusing various Chou's pseudo components and using wavelet denoising approach. *J Theor Biol* 462 (2019) 329–346.
- [221] L. Zhang, L. Kong, iRSpot-PDI: Identification of recombination spots by incorporating dinucleotide property diversity information into Chou's pseudo components. *Genomics* 111 (2019) 457–464.
- [222] S. Zhang, K. Yang, Y. Lei, K. Song, iRSpot-DTS: Predict recombination spots by incorporating the dinucleotide-based spare-cross covariance information into Chou's pseudo components. *Genomics* 111 (2019) 1760–1770.
- [223] K.C. Chou, Two kinds of metrics for computational biology. *Genomics* <https://www.sciencedirect.com/science/article/pii/S0888754319304604?via%3Dihub> (2019).
- [224] K.C. Chou, Proposing pseudo amino acid components is an important milestone for proteome and genome analyses. *International Journal for Peptide Research and Therapeutics (IJPR)* <https://doi.org/10.1007/s10989-019-09910-7> or <https://link.springer.com/article/10.1007%2Fs10989-019-09910-7> (2019).

- [225] K.C. Chou, An insightful recollection for predicting protein subcellular locations in multi-label systems. *Genomics* <http://doi.org/10.1016/j.ygeno.2019.08.008> or <https://www.sciencedirect.com/science/article/pii/S0888754319304604?via%3Dihub> (2019).
- [226] K.C. Chou, Progresses in predicting post-translational modification. *International Journal of Peptide Research and Therapeutics (IJPRT)* <https://doi.org/10.1007/s10989-019-09893-5> or <https://link.springer.com/article/10.1007%2Fs10989-019-09893-5> (2019).
- [227] K.C. Chou, Recent Progresses in Predicting Protein Subcellular Localization with Artificial Intelligence (AI) Tools Developed Via the 5-Steps Rule. *Japanese Journal of Gastroenterology and Hepatology* <https://doi.org/www.jjgastrohepto.org> or <https://www.jjgastrohepto.org> (2019).
- [228] K.C. Chou, An insightful recollection since the distorted key theory was born about 23 years ago. *Genomics* <https://doi.org/10.1016/j.ygeno.2019.09.001> or <https://www.sciencedirect.com/science/article/pii/S0888754319305543?via%3Dihub> (2019).
- [229] K.C. Chou, Artificial intelligence (AI) tools constructed via the 5-steps rule for predicting post-translational modifications. *Trends in Artificial Intelligence (TIA)* 3 (2019) 60–74.
- [230] K.C. Chou, Distorted Key Theory and Its Implication for Drug Development. *Current Genomics* <http://www.eurekaselect.com/175823/article> or <http://www.eurekaselect.com/175823/article> (2020).
- [231] K. C. Chou, An Insightful 10-year Recollection Since the Emergence of the 5-steps Rule. *Current Pharmaceutical Design* 2019, 25, 4223–4234.
- [232] K.C. Chou, An insightful recollection since the birth of Gordon Life Science Institute about 17 years ago. *Advancement in Scientific and Engineering Research* 4 (2019) 31–36.
- [233] K.C. Chou, Gordon Life Science Institute: Its philosophy, achievements, and perspective. *Annals of Cancer Therapy and Pharmacology* 2 (2019) 001–26.

***Corresponding authors:** Kuo-Chen Chou, Gordon Life Science Institute, Boston, Massachusetts 02478, USA;

Email: kcchou@gordonlifescience.org or kcchou38@gmail.com