doi:10.20944/preprints202011.0297.v1

Linear Regression Analysis for Time-Point Datasets

Janardan Patil*, Li Len, Abhinav Bharat, and Xi Li
Department of Computer Science, Nagpur University, India 560987
*Email: jpatilnagpuredu@gmail.com
Phone: +91 9877659876

Abstract

In this paper, we present a relapse based demonstrating way to deal with investigate various arrangement MTC information. A commonplace use of this displaying approach incorporates three stages: first, define a model that approximates the connection between quality articulation and trial factors, with boundaries consolidated to address the exploration premium; second, utilize least-squares and assessing condition methods to gauge boundaries and their relating standard blunders; third, register test insights, P-qualities and NFD as proportions of factual criticalness. The benefits of this methodology are as per the following. To begin with, it tends to the exploration interest in a particular, precise way, and maximally uses all the information and other important data. Second, it represents both orderly and irregular varieties related with the information, and the consequences of such examination give not just quality explicit data applicable to the exploration objective, yet additionally its dependability, in this way helping agents to settle on better choices for subsequent investigations. Third, this methodology is truly adaptable, and can undoubtedly be stretched out to different sorts of MTC considers or other microarray explores by detailing various models dependent on the test plan of the investigations.

Keywords: Regression, time point data, modelling.

INTRODUCTION

Microarray time course (MTC) studies can be generally ordered into four basic sorts: single-arrangement and various arrangement, each with and without time-changing cofactors. A regular single-arrangement MTC study utilizes one microarray slide (and its duplicates) to gauge articulation profiles at each time point. The essential goal in these single-arrangement MTC contemplates is to describe the fleeting examples of quality articulation (changes). Instances of such a solitary arrangement MTC try incorporate the yeast cell cycle concentrate by Cho et al. (1-10), which estimated the articulation profiles of one example (the coordinated yeast societies) after some time on high-thickness oligonucleotide exhibits, and the fibroblast serum incitement reaction concentrate by Iyer et al. (2), which observed the adjustments in articulation profiles of one sets of tests—the serum-invigorated fibroblasts (therapy gathering) and the peaceful fibroblasts (control gathering) that were seriously hybridized onto a similar cDNA cluster—and estimated the proportions of their fluorescence forces over the long haul. Interestingly, an average numerous arrangement MTC study uses various microarray slides at each time point, hybridized with various examples—for instance, at least one freaks versus a wild-type control, or diverse medication treatment bunches versus a fake treatment or false treated control.

Right now, group examination, which is normally used to break down information from different investigations utilizing microarray innovations (3–7), is additionally most oftentimes used to dissect MTC information (1,2,8–50). In MTC considers, an ordinary bunch investigation figures pairwise connections (or some other separation measures) among qualities, at that point bunches qualities into groups (12,13) or various leveled trees (14) without using timing data. When the groups are shaped, the normal of the articulation estimations of the qualities inside the bunch is figured and outwardly showed to survey designs related with timing. The critical quality of bunch examination is to amass qualities so one can envision important examples (50-100). Notwithstanding, bunch investigation has a few shortcomings significant. To start with, the circumstance data or any time-shifting cofactors are not joined in the investigation. Second, a commonplace group investigation doesn't quantify measurable noteworthiness, in that it will consistently discover bunches whether or not or not important groups exist. Third, group participations are effortlessly impacted by selection of scales, changes or sifting measures.

While trying to comprehend the early functions during HD pathogenesis, striatal RNAs were extricated from the cerebrums of these mice at different timepoints, when the enlistment of the freak htt, and afterward hybridized to Affymetrix Mu11K oligonucleotide exhibits. Beginning assessment of the information uncovered that quality articulation changes in this model were subtler than those in a past HD mouse model (100-140) (R. Luthi-Carter and J. Olson, unpublished perception). Utilizing the factual demonstrating approach depicted here, we endeavor to recognize bestcandidate qualities that are differentially communicated between the freak and control mice, and assess their measurable importance. This paper centers around factual strategies for MTC examines. The total dataset, affirmation examines and organic understanding will be introduced in another article.

METHOD & RESULTS

So as to pick up experiences into the pathogenesis components of poly(Q) expansion in huntingtin, RNA were set up from the striata of HD94 mice (24) or the single transgenic control mice conveying the tTA atom (tTA control) at the next weeks: 2, 1.5, 1, 0, 2, 4, 6 and 8, with week 0 as the hour of enlistment (Table 1). These were hybridized to Affymetrix Mu11K Sub B oligonucleotide clusters (subtleties are depicted in Materials and Methods). The essential objective of this examination is to recognize qualities that are communicated differentially between the control and the freak mice over the long run after the acceptance of freak htt. To accomplish this objective, the relapse model should consolidate boundaries that explicitly address the exploration interest, while simultaneously using all accessible applicable data (141-180). The articulation profile produced from every hybridization can be conceptualized as a vector of J reactions. Let Yk ¼ (Y1k, Y2k, ... ,YJk) 0 mean the articulation profile created from the kth hybridization, where Yjk indicates the declaration of the jth quality in the kth profile (j ¼ 1, 2, ... ,J; k ¼ 1, 2, ... ,K). Two snippets of data with respect to the example utilized in the kth hybridization are pertinent to the exploration objective: the genotype of the mouse from which the example was taken, and the timepoint throughout acceptance when the example was gathered (recorded in Table 1).

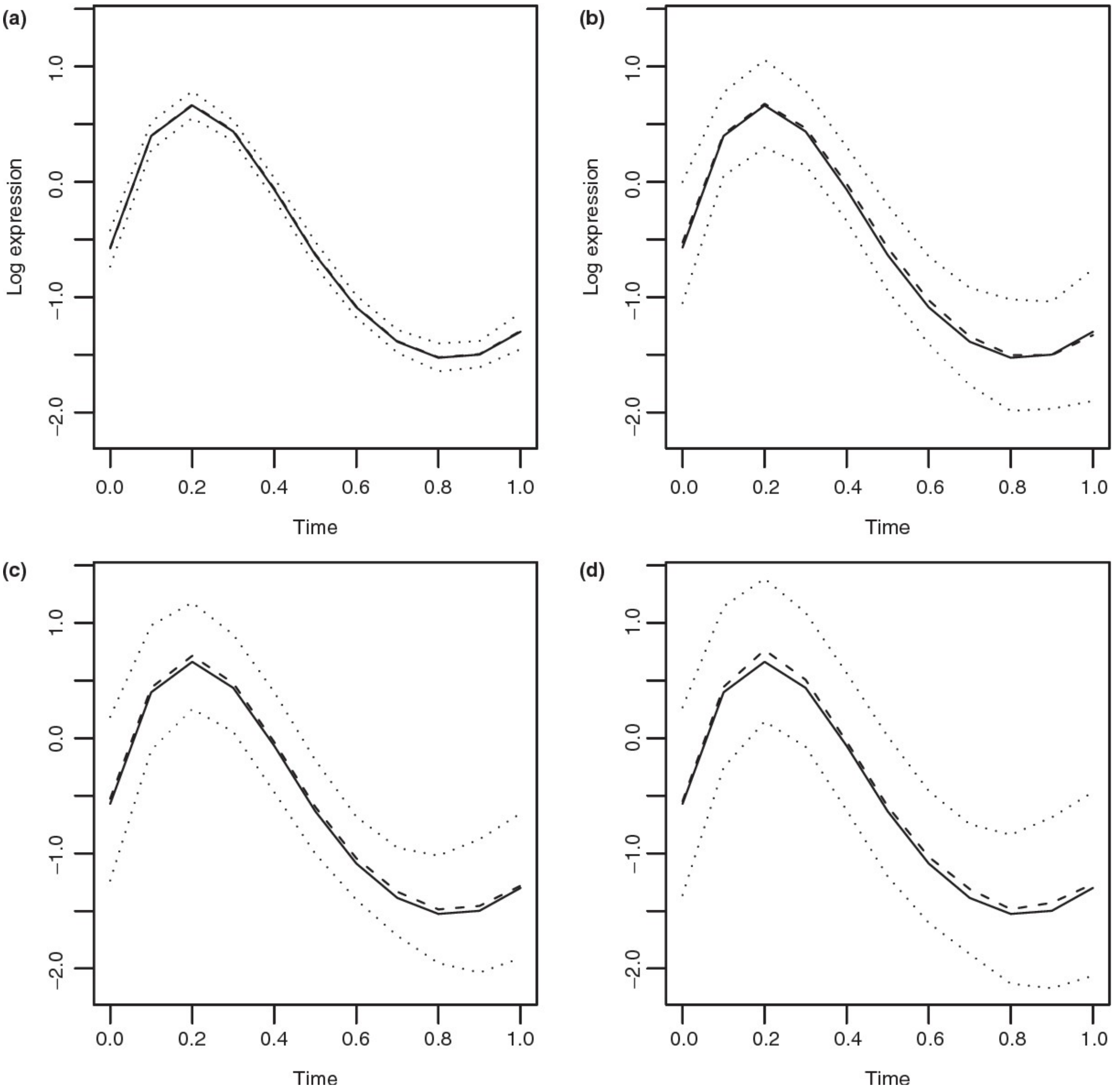

Figure1: Regression with predictor variable, time.

Notwithstanding utilizing the crude articulation esteems, we likewise changed them to rank scores, that is, we supplanted the genuine articulation esteems by their positions (from 1 to 2143) as portrayed by C. Cheng, R. Kimmel, P. Neiman and L.P. Zhao (composition in arrangement). The upsides of utilizing rank scores are (I) the change naturally changes for the methodical heterogeneity among tests, hence making outcomes more steady, and (ii) the outcomes won't be altogether impacted by qualities with uncommonly enormous articulation esteems. The hindrance is that the rank change loses some level of quantitative data. Figure 4 shows an ordinary monotonic connection between rank scores and crude articulation esteems. As appeared, the huge articulation esteems were downsized after position change. Since the utilization of positions naturally changes for heterogeneity, the variables (dk, lk) were set to (0,

1) in the model.

Utilizing a similar assessment and induction method, we got a bunch of test measurements utilizing Equation 2 and figured their comparing P-values. As specific illustrations, Figure 5 shows the six qualities with the best or negative Zwj , Zkj or ZZj , determined from the rank scores of the dataset. Contrasting and the crude information, the utilization of rank scores created more competitor qualities at $P < 0.1$ (jZj > 4.994): 1 essentially unique at capture wj, 32 at incline kj (2 cover with the 7 up-and-comer qualities got from the crude information) and 3 at quadratic coefficient Zj. A sum of 36 interesting qualities were recognized at this noteworthiness level (Table 3). As likewise appeared in another examination (C. Cheng, R. Kimmel, P. Neiman and L.P. Zhao, composition in planning), rank change seemed to expand the intensity of investigation because of decreasing varieties in the crude information, when heterogeneities among information are huge (181-194).

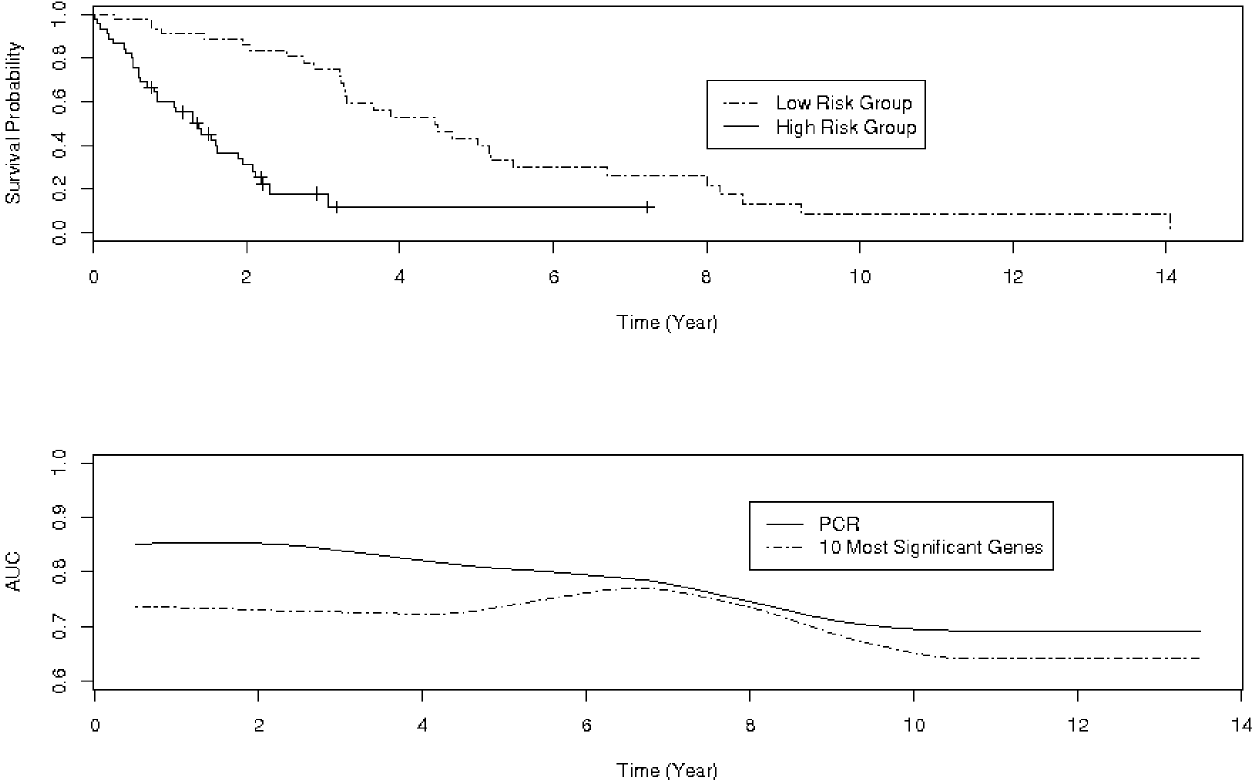

Figure 2: Survival analysis on selected genes.

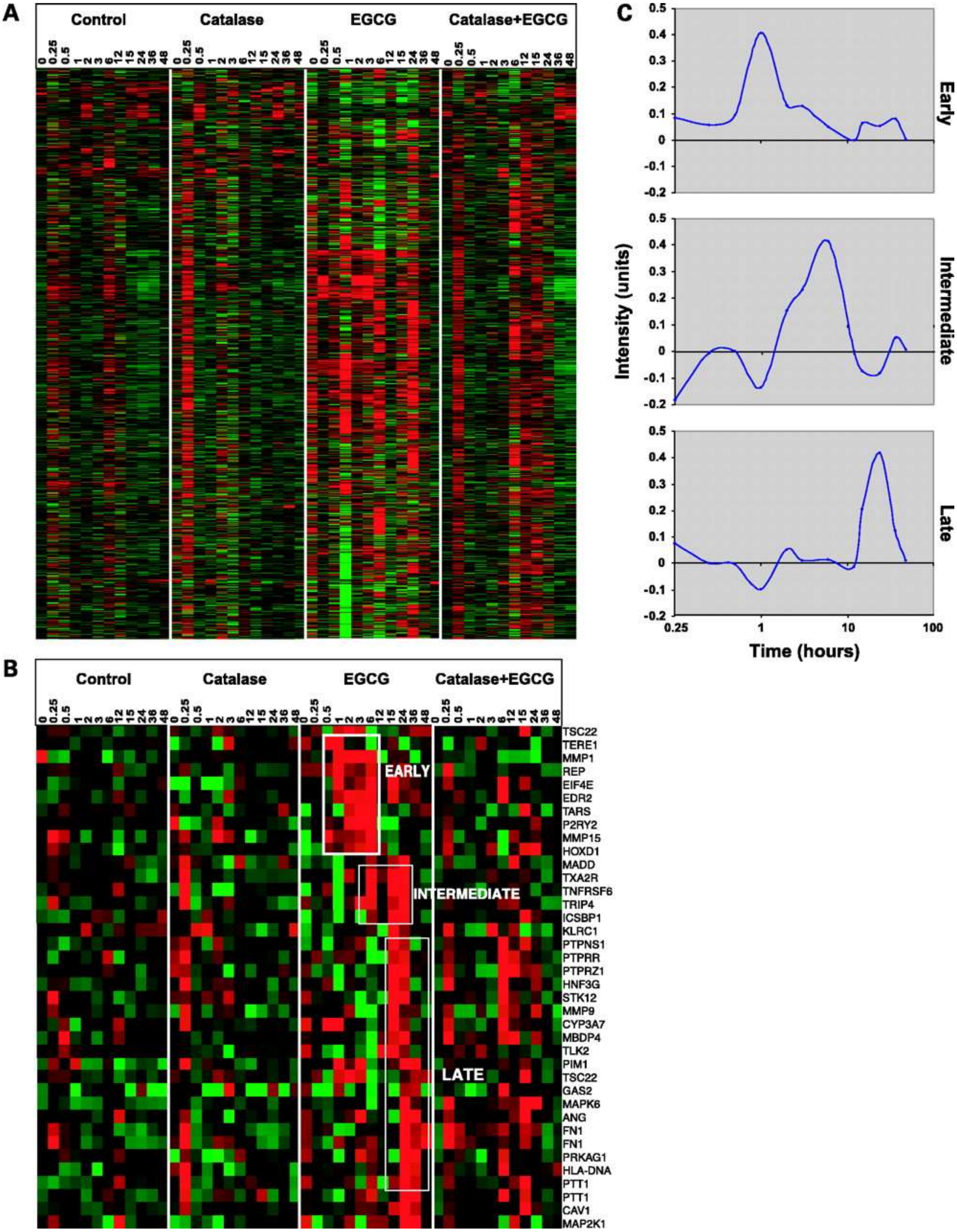

Figure 3: Heat map of expression from significant genes.

To ascertain NFD at a specific limit of the test measurement, we followed similar registering methods as depicted above on each permutated dataset: successively fitting the model in a forward stepwise manner, utilizing either the crude information or the rank scores, and processing permutated Zwj , Zkj or ZZj insights. At each progression of model-fitting, we tallied the quantity of qualities with outright estimations of Zwj , Zkj or ZZj surpassing a specific limit Z0. The normal NFD for each progression is the normal of such checks over all the permutated datasets. Moreover, to assess the all out number of qualities that were fundamentally unique between the HD94 mice and the tTA controls, paying little mind to which boundary was thought of, we checked the quantity of qualities with any Zwj , Zkj or ZZj surpassing the edge Z0 in each permuted dataset, and, as over, the normal absolute NFD is the normal of such tallies over all the permutated datasets. For instance, Table 4 shows the normal NFD for Zkj and the normal absolute NFD at various limits Z0, contrasted and the quantity of applicant qualities recognized in the genuine dataset (the two of which were determined from the rank scores).

DISCUSSION

In this paper, we present a relapse based displaying way to deal with dissect different arrangement MTC information. A common use of this demonstrating approach incorporates three stages: first, figure a model that approximates the connection between quality articulation and exploratory components, with boundaries consolidated to address the examination premium; second, utilize least-squares and assessing condition procedures to appraise boundaries and their comparing standard mistakes; third, register test insights, P-qualities and NFD as proportions of factual essentialness. The upsides of this methodology are as per the following. To begin with, it tends to the examination interest in a particular, methodical way, and maximally uses all the information and other important data. Second, it represents both deliberate and arbitrary varieties related with the information, and the consequences of such examination give not just quality explicit data applicable to the exploration objective, yet in addition its dependability, accordingly helping agents to settle on better choices for subsequent investigations. Third, this methodology is truly adaptable, and can without much of a stretch be reached out to different kinds of MTC examines or other microarray tests by detailing various models dependent on the trial plan of the examinations. In the current application, we set up a request for qualities that may communicate differentially among HD94 and control mice during the time course under examination, in light of the scores of Z-insights (Zwj , Zkj or ZZj). These can fill in as possibility for additional examinations. Predictable with the underlying perception (R. Luthi-Carter and J. Olson, unpublished outcome), the progressions distinguished on these qualities were gentle. In any case, a small amount of them were factually critical, and, from a measurable perspective, almost certainly, with extra imitates and a bigger example size, or zeroing in on a more modest arrangement of qualities, more competitor qualities with unassuming changes can be recognized as factually huge.

Logarithmic change is frequently acted in microarray information examination. For datasets created utilizing clusters with an Affymetrix stage, for example, this one, it is important to eliminate or recode an enormous division of information with negative qualities before logarithmic change, and the measurable results of such recoding of unique information are not satisfactory. The rank change system portrayed above can fill in as an elective change, which likewise all the while changes for the heterogeneity. In this dataset, results got from logarithmically changed information to a great extent covered with those from those utilizing rank-changed (information not appeared). The two investigations gave off an impression of being more remarkable than utilization of the crude information, most likely inferable from decreased heterogeneity and exception impacts.

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

REFERENCES

1. Yu R, Li D, Du X, Xia S, Liu C, Shi G (2017) Comparative transcriptome analysis reveals key cadmium transport-related genes in roots of two pakchoi (Brassica rapa L. ssp. chinensis) cultivars. BMC Genomics 18:587
2. Yusuf M, Fariduddin Q, Ahmad A (2012) 24-Epibrassinolide modulates growth, nodulation, antioxidant system, and osmolyte in tolerant and sensitive varieties of Vignaradiata under different levels of nickel: a shotgun approach. Plant Physiol Biochem 57:143–153
3. Lei Nie, Gang Wu, Weiwen Zhang. "Correlation of mRNA Expression and Protein Abundance Affected by Multiple Sequence Features Related to Translational Efficiency in Desulfovibrio vulgaris: A Quantitative Analysis". Genetics Society of America. 2006;174 :2229–2243.
4. Simon Rogers, Mark Girolami, Walter Kolch, Katrina M Waters, Tao Liu, Brian Thrall, H Steven Wiley. "Investigating the correspondence between transcriptomic and proteomic expression profiles using coupled cluster models" Bioinformatics . 2008;24 :2894– 2900.
5. S Liang, S Fuhrman, R Somogyi. "Reveal, a general reverse engineering algorithm for inference of genetic network architectures" Pacific Symposium on Biocomputing . 1998;3 (3):18–29.
6. P D'haeseleer. "Linear modeling of mrna expression levels during cns development and injury" Pacific Symposium on Biocomputing. 1999;4 :41–52.
7. Reinhard Guthke, Ulrich Möller, Martin Hoffmann, Frank Thies, Susanne Töpfer. "Dynamic network reconstruction from gene expression data applied to immune response during bacterial infection" Bioinformatics. 2005;21(8):1626–1634.
8. Edward R Dougherty. "Validation of inference procedures for gene regulatory networks" Current Genomics. 2007;8(6):351–359.
9. N Friedman, M Linial, I Nachman, D Pe'er. "Bayesian networks to analyze expression data" Proceedings of the Fourth Annual International Conference on Computational Molecular Biology . 2000:127–135.
10. N Nariai, S Kim, S Imoto, S Miyano. "Using protein-protein interactions for refining gene networks estimated from microarray data by bayesian networks" Pacific Symposium on Biocomputing . 2004;9 :336–347.
11. Yu Zhang, Zhidong Deng , Hongshan Jiang, Peifa Jia. "Inferring gene regulatory networks from multiple data sources via a dynamic bayesian network with structural em" Data Integration in the Life Sciences. 2007;4544 :204–214.
12. Pawar, S., Donthamsetty, S., Pannu, V., Rida, P., Ogden, A., Bowen, N., Osan, R., Cantuaria, G., and Aneja, R. (2014) KIFCI, a novel putative prognostic biomarker for ovarian adenocarcinomas: delineating protein interaction networks and signaling circuitries. J. Ovarian Res. 7, 53
13. Adriano V Werhli, Dirk Husmeier. "Reconstructing gene regulatory networks with bayesian networks by combining expression data with multiple sources of prior knowledge" Statistical Applications in Genetics and Molecular Biology . 2007;6 (15)
14. Lux A, Martinka M, Vaculık M, White PJ (2011) Root responses to cadmium in the rhizosphere: a review. J Exp Bot 62:21–37. https://doi.org/10.1093/jxb/erq281
15. Lv Y, Deng X, Quan L, Xia Y, Shen Z (2013) Metallothioneins BcMT1 and BcMT2 from Brassica campestris enhance tolerance to cadmium and copper and decrease production of reactive oxygen species in Arabidopsis thaliana. Plant Soil 367:507–519
16. Maestri E, Marmiroli M, Visioli G, Marmiroli N (2010) Metal tolerance and hyperaccumulation: costs and trade-offs between traits and environment. Environ Exp Bot 68:1–13. https://doi.org/10.1016/j.envexpbot.2009.10.011
17. Maggio A, Joly RJ (1995) Effects of mercuric chloride on the hydraulic conductivity of tomato root systems (evidence for a channel-mediated water pathway). Plant Physiol 109:331–335
18. Batra, H.; Pawar, S.; Bahl, D. Curcumin in combination with anti-cancer drugs: A nanomedicine review. Pharm. Res. 2018, 139, 91–105.
19. Malar S, Vikram SS, Favas PJC, Perumal V (2014) Lead heavy metal toxicity induced changes on growth and antioxidative enzymes level in water hyacinths [Eichhorniacrassipes (Mart.)]. Bot Stud 55:54
20. Manara A (2012) Plant responses to heavy metal toxicity. In: Furini A (ed) Plants and heavy metals, Springer briefs in molecular science. Springer, Dordrecht, pp 27–53
21. Margoshes M, Valle BL (1957) A cadmium protein from equine kidney cortex. J Am Chem Soc 79:4813–4814
22. Marschner H (1995) Mineral nutrition of higher plants, 2nd edn. Academic Press, London, pp 405 435
23. Mehes-Smith M, Nkongolo K, Cholewa E (2013) Coping mechanisms of plants to metal contaminated soil. In: Steven S (ed) Environmental change and sustainability, InTech Open, London, UK. https://doi.org/10.5772/55124.8
Mehra RK, Winge DR (1988) Cu(I) binding to the Saccharomyces pombe γ-glutamylpeptides varying in chain lengths. Arch Biochem Biophys 265:381–389

24. Mendoza-Cózatl DG, Butko E, Springer F, Torpey JW, Komives EA, Kehr J, Schroeder JI (2008) Identification of high levels of phytochelatins, glutathione and cadmium in the phloem sap of Brassica napus. A role for thiol peptides in the long-distance transport of cadmium and the effect of cadmium on iron translocation. Plant J 54:249–259
25. Meuwly P, Thibault P, Rauser WE (1993) γ-Glutamylcysteinyl glutamic acid; a new homologue of glutathione in maize seedlings exposed to cadmium. FEBS Lett 336:472–476
26.Meuwly P, Thibault P, Schwan AL, Rauser WE (1995) Three families of thiol peptides are induced by cadmium in maize. Plant J 7:391–400
27. Mir G, Domènech J, Huguet G, Guo WJ, Goldsbrough P, Atrian S, Molinas M (2004) A plant type 2 metallothionein (MT) from cork tissue responds to oxidative stress. J Exp Bot 55:2483–2493
28. Mittal, K., Choi, D.H., Klimov, S. et al. A centrosome clustering protein, KIFC1, predicts aggressive disease course in serous ovarian adenocarcinomas. J Ovarian Res 9, 17 (2016). https://doi.org/10.1186/s13048-016-0224-0
29. Ashraf, M. I., Ong, S. K., Mujawar, S., Pawar, S., More, P., Paul, S., et al. (2018). A side-effect free method for identifying cancer drug targets. Sci. Rep. 8:6669. doi: 10.1038/s41598-018-25042-2
30. Montargès-Pelletier E, Chardot V, Echevarria G, Michot LJ, Bauer A, Morel JL (2008) Identification of nickel chelators in three hyperaccumulating plants: an X-ray spectroscopic study. Phytochemistry 69:1695–1709
31. Morelli E, Scarano G (2001) Synthesis and stability of phytochelatins induced by cadmium and lead in the marine diatom Phaeodactylum tricornutum. Mar Environ Res 52:383–395. https://doi.org/10.1016/S0141-1136(01)00093-9
32. E Segal, H Wang, D Koller. “Discovering molecular pathways from protein interaction and gene expression data” Bioinformatics . 2003;19 (1):i264–i272.
33. Takakazu Kaneko, Yasukazu Nakamura, Shusei Sato, Kiwamu Minamisawa, Toshiki Uchiumi, Shigemi Sasamoto, Akiko Watanabe, Kumi Idesawa, Mayumi Iriguchi, Kumiko Kawashima, Mitsuyo Kohara, Midori Matsumoto, Sayaka Shimpo, Hisae Tsuruoka, Tsuyuko Wada, Manabu Yamada, Satoshi Tabata. “Complete genomic sequence of nitrogen-fixing symbiotic bacterium bradyrhizobium japonicum usda110” DNA Research . 2002;9 :189–197.
34. David N Perkins, Darryl J C Pappin, David M Creasy, John S Cottrell. “Probability-based protein identification by searching sequence databases using mass spectrometry data” ELECTROPHORESIS . 1999;20 (18):3551–3567.
35. G Pessi, C H Ahrens, H Rehrauer, A Lindemann. “Genome-wide transcript analysis of Bradyrhizobium japonicum bacteroids: in soybean root nodules” Mol. Plant Microb Interact . 2007;20 :1353–1363.
36. Annamraju D Sarma, David W Emerich. “Global protein expression pattern of bradyrhizobium japonicum bacteroids: A prelude to functional proteomics". PROTEOMICS . 2005;5 (16):4170–4184.
37. Schmid H, Boucherot A, Yasuda Y, Henger A, Brunner B, Eichinger F, Nitsche A, Kiss E, Bleich M, Gröne HJ, Nelson PJ, Schlöndorff D, Cohen CD, Kretzler M. “Modular activation of nuclear factor-kappab transcriptional programs in human diabetic nephropathy” Diabetes . 2006;55(11):2993–3003.
38. Hans J Baelde, Michael Eikmans , Peter P Doran, David WP Lappin, Emile de Heer, Jan A. Bruijn, “Gene expression profiling in glomeruli from human kidneys with diabetic nephropathy” American Journal of Kidney Dis-eases. 2004;43 (4):636–650.
39. M Rudnicki, S Eder, P Perco, J Enrich, K Scheiber, C Koppelstatter, G Schratzberger, B Mayer, R Oberbauer, T W Meyer, G Mayer. “Gene expression profiles of human proximal tubular epithelial cells in proteinuric nephropathies” Kidney Int. 2006;71 :325–335.
40. Amos Bairoch, Brigitte Boeckmann, Serenella Ferro, Elisabeth Gasteiger. “Swiss-prot: Juggling between evolution and stability” Briefings in Bioinformatics . 2004;5 (1):39–55.
41. Paul D Thomas, Anish Kejariwal , Michael J Campbell, Huaiyu Mi, Karen Diemer, Nan Guo, Istvan Ladunga, Betty Ulitsky-Lazareva, Anushya Muruganujan, Steven Rabkin, Jody A Vandergriff , Olivier Doremieux. “Panther a browsable database of gene products organized by biological function, using curated protein family and subfamily classification” Nucleic Acids Research . 2003;31(1):334–341.
42. Huaiyu Mi, Qing Dong, Anushya Muruganujan, Pascale Gaudet, Suzanna Lewis, Paul D Thomas. “Panther version 7: improved phylogenetic trees, orthologs and collaboration with the gene ontology consortium” Nucleic Acids Research. 2010;38 (suppl 1):D204–D210.
43. Lahiri, C., Pawar, S., Sabarinathan, R., Ashraf, M. I., Chand, Y., and Chakravortty, D. (2014). Interactome analyses of Salmonella pathogenicity islands reveal SicA indispensable for virulence. J. Theor. Biol. 363, 188–197. doi: 10.1016/j.jtbi.2014.08.013
44. Da Wei Huang, Brad T Sherman, Richard A Lempicki. “Systematic and integrative analysis of large gene lists using david bioinformatics resources” Nature Protocols . 2008;4 :44–57.
45. Andreas Bernthaler, Irmgard Muhlberger, Raul Fechete, Paul Perco, Arno Lukas, Bernd Mayer. “A dependency graph approach for the analysis of differential gene expression profiles” Mol. BioSyst . 2009;5 :1720–1731.
46. Voichita D Marinescu, Isaac S Kohane, Alberto Riva. “The mapper database: a multi-genome catalog of putative transcription factor binding sites” Nucleic Acids Research . 2005;33(suppl 1):D91–D97.
47. Yuri Nikolsky, Evgeny Sviridov, Jun Yao, Damir Dosymbekov, Vadim Ustyansky, Valery Kaznacheev, Zoltan Dezso, Laura Mulvey, Laura E Macconaill, Wendy Winckler , Tatiana Serebryiskaya , Tatiana Nikolskaya , Kornelia Polyak. “Genome-wide functional synergy between amplified and mutated genes in human breast cancer” Cancer Research . 2008;68(22):9532–9540.
48. Zoltan Dezso, Yuri Nikolsky, Tatiana Nikolskaya, Jeremy Miller, David Cherba, Craig Webb, Andrej Bugrim. “Identifying disease-specific genes based on their topological significance in protein networks” BMC Syst Biol . 2009;3 (36)
49. Vasyl Pihur, Susmita Datta, Somnath Datta. “Rankaggreg, an r package for weighted rank aggregation” BMC Bioin-formatics . 2009;10(1):62.

50. RY Rubinstein, DP Kroese. The Cross-Entropy Method: A Unified Approach to Combinatorial Optimization, Monte-Carlo Simulation and Machine Learning. New York : Springer-Verlag ; 2004.

51. Pawar S, Ashraf MI, Mujawar S, Mishra R and Lahiri C (2018) In silico Identification of the Indispensable Quorum Sensing Proteins of Multidrug Resistant Proteus mirabilis. Front. Cell. Infect. Microbiol. 8:269. doi: 10.3389/fcimb.2018.00269

52. Holstege FC, Jennings EG, Wyrick JJ, Lee TI, Hengartner CJ, Green MR, Golub TR, Lander ES, Young RA. "Dissecting the regulatory circuitry of a eukaryotic genome" Cell . 1998; 95 :717–728.

53. Frederick P Roth, Jason D Hughes, Preston W Estep, George M Church. "Finding dna regulatory motifs within unaligned noncoding sequences clustered by whole-genome mrna quantitation" Nat Biotech . 1998;16 :939–945.

54. Scott A Jelinsky, Leona D Samson. "Global response of saccharomyces cerevisiae to an alkylating agent" Proceedings of the National Academy of Sciences . 1999;96(4):1486–1491.

55. Velculescu VE, Zhang L, Zhou W, Vogelstein J, Basrai MA, Bassett DE, Jr, Hieter P, Vogelstein B, Kinzler KW. "Characterization of the yeast transcriptome" Cell . 1997;88 :243–251.

56. Futcher B, Latter GI, Monardo P, McLaughlin CS, Garrels JI. "A sampling of the yeast proteome" Mol Cell Biol. 1999;19 :7357–7368.

57. Washburn MP, Wolters D, Yates JR., 3rd "Large-scale analysis of the yeast proteome by multidimensional protein identification technology" Nat Biotechnol . 2001;19 :242–247.

58. Peng J, Elias JE, Thoreen CC, Licklider LJ, Gygi SP. "Evaluation of multidimensional chromatography coupled with tandem mass spectrometry (LC/LC-MS/MS) for large-scale protein analysis the yeast proteome" J Proteome Res . 2003;2 (2):43–50.

59. Jerome H Friedman. "Greedy function approximation: A gradient boosting machine". The Annals of Statistics. 2001;29 (5):1189–1232.

60. John F Heidelberg, Rekha Seshadri , Shelley A Haveman, Christopher L Hemme, Ian T Paulsen, James F Kolonay, Jonathan A Eisen, Naomi Ward, Barbara Methe, Lauren M Brinkac, Sean C Daugherty, Robert T Deboy, Dodson, Robert J, A Scott Durkin, Ramana Madupu, William C Nelson, Steven A Sullivan, Derrick Fouts , Daniel H Haft, Jeremy Selengut, Jeremy D Peterson, Tanja M Davidsen, Nikhat Zafar, Liwei Zhou, Diana Radune, George Dimitrov, Mark Hance, Kevin Tran, Hoda Khouri, John Gill, Terry R Utterback, Tamara V Feldblyum, Judy D Wall, Gerrit Voordouw , Claire M Fraser. "The genome sequence of the anaerobic, sulfate-reducing bacterium desulfovibrio vulgaris hildenborough" Nat Biotech . 2004;22 :554–559.

61. Pawar S, Stanam A, Chaudhari M, Rayudu D. Effects of temperature on COVID-19 transmission. medRxiv. doi: https://doi.org/10.1101/2020.03.29.20044461

62. Lei Nie, Gang Wu, Weiwen Zhang. "Correlation between mrna and protein abundance in desulfovibrio vulgaris: A multiple regression to identify sources of variations". Biochemical and Biophysical Research Communications. 2006;339(2):603–610.

63. Richard G Lomax. Statistical Concepts: A Second Course for Education and the Behavioral Sciencess. New York: Longman; 1992.

64. Bruce G Lindsay. "Mixture models: Theory, geometry and applications" NSF-CBMS Regional Conference Series in Probability and Statistics . 1995;5 :iiii+v-ix+1–163.

65. A P Dempster, N M Laird, D B Rubin. "Maximum likelihood from incomplete data via the em algorithm," Journal of the Royal Statistical Society Series B (Methodological) . 1977;39 (1):1–38.

66. Marina Meila. "Comparing clusterings—an information based distance" Journal of Multivariate Analysis. 2007;98(5):873–895.

67. Gideon Schwarz. "Estimating the dimension of a model" The Annals of Statistics . 1978;6(2):461–464.

68. Darya Chudova, Christopher Hart, Eric Mjolsness, Padhraic Smyth. "Gene expression clustering with functional mixture models" Advances in Neural Information Processing Systems . 2004;16

69. Yihui Luan, Hongzhe Li. "Clustering of time-course gene expression data using a mixed-effects model with b-splines" Bioinformatics . 2003;19 (4):474–482.

70. Paul T Spellman, Gavin Sherlock, Michael Q Zhang, Vishwanath R Iyer, Kirk Anders , Michael B Eisen, Patrick O Brown, David Botstein, Bruce Futcher. "Comprehensive identification of cell cycle-regulated genes of the yeast saccharomyces cerevisiae by microarray hybridization" Molecular Biology of the Cell . 1998;9 (12):3273–3297.

71. H W Mewes, D Frishman, U Güldener, G Mannhaupt, K Mayer, M Mokrejs, B Morgenstern, M Münsterkötter, S Rudd, B Weil. "Mips: a database for genomes and protein sequences" Nucleic Acids Research . 2002;30 (1):31–34.

72. Pawar, S.; Lahiri, C. Quorum sensing: An imperative longevity weapon in Bacteria. Afr J Microbiol Res 2018, 12, 96-104. DOI: 10.5897/AJMR2017.8751.

73. Degeng Wang. "Discrepancy between mrna and protein abundance: Insight from information retrieval process in computers". Computational Biology and Chemistry. 2008;32 (6):462–468.

74. Alain Barrat, Marc Barthlemy, Alessandro Vespignani. Dynamical Processes on Complex Networks. New York, NY USA: Cambridge University Press; 2008.

75. Yong-Yeol Ahn, James P Bagrow, Sune Lehmann. "Link communities reveal multiscale complexity in networks" Nature. 2010 Jun;466 (7307):761–764.

76. Andrea Lancichinetti, Mikko Kivelä , Jari Saramäki, Santo Fortunato. "Characterizing the community structure of complex networks" PLOSOne . 2010;5(8):e11976–1-8.

77. Chen Y, Zhi J, Zhang H, Li J, Zhao Q, Xu J (2017) Transcriptome analysis of Phytolaccaamericana L. in response to cadmium stress. PLoS One 12(9):e0184681

78. Chia MA, Lombardi AT, Melão MGG, Parrish C (2015) Combined nitrogen limitation and cadmium stress stimulate total carbohydrates, lipids, protein and amino acid accumulation in Chlorella vulgaris (Trebouxiophyceae). Aquat Toxicol 160:87–95

79. Clemens S (2006) Toxic metal accumulation, responses to exposure and mechanisms of tolerance in plants. Biochimie 88:1707–1719

80. Cobbett C, Goldsbrough P (2002) Phytochelatins and metallothioneins: roles in heavy metal detoxification and homeostasis. Annu Rev Plant Biol 53:159–182

81. Collin VC, Eymery F, Genty B, Rey P, Havaux M (2008) Vitamin E is essential for the tolerance of Arabidopsis thaliana to metal induced oxidative stress. Plant Cell Environ 31:244–8257

82. Cuypers A, Smeets K, Vangronsveld J (2009) Heavy metal stress in plants. In: Hirt H (ed) Plant stress biology: from genomics to systems biology. Wiley-VCH Verlag, Weinheim, pp 161–178

83. Dago A, Gonzalez I, Arino C, Diaz-Cruz JM, Esteban M (2014) Chemometrics applied to the analysis of induced phytochelatins in Hordeum vulgare plants stressed with various toxic non-essential metals and metalloids. Talanta 118:201–209. https://doi.org/10.1016/j.talanta.2013.09.058

84. DalCorso G, Farinati S, Maistri S, Furini A (2008) How plants cope with cadmium: staking all on metabolism and gene expression. J Integr Plant Biol 50:1268–1280

85. DalCorso G, Fasani E, Furini A (2013) Recent advances in the analysis of metal hyperaccumulation and hypertolerance in plants using proteomics. Front Plant Sci 4:280

86. Dalvi AA, Bhalerao SA (2013) Response of plants towards heavy metal toxicity: an overview of avoidance, tolerance and uptake mechanism. Annals of Plant Sciences 2:362–368

87. Pawar, S., Ashraf, M. I., Mehata, K. M., and Lahiri, C. (2017). "Computational identification of indispensable virulent proteins of Salmonella Typhi CT18," in Current Topics in Salmonella and Salmonellosis, ed M. Mares (InTech Publishers), 21–39.

88. Grill E, Gekeler W, Winnacker E-L, Zenk MH (1986) Homo-phytochelatins are heavy metal-binding peptides of homo-glutathione containing Fabales. FEBS Lett 205:47–50

89. Grill E, Loffler S, Winnacker EL, Zenk MH (1989) Phytochelatins, the heavy-metal-binding peptides of plants, are synthesized from glutathione by a specific gamma-glutamyl cysteine dipeptidyltranspeptidase (phytochelatin synthase). Proc Natl Acad Sci U S A 86:6838–6842

90. Guerinot ML (2000) The ZIP family of metal transporters. Biochim Biophys Acta 1465:190–198. https://doi.org/10.1016/S0005-2736(00)00138-3

91. Guo WJ, Bundithya W, Goldsbrough PB (2003) Characterization of the Arabidopsis metallothionein gene family: tissue-specific expression and induction during senescence and in response to copper. New Phytol 159:369–381. https://doi.org/10.1046/j.1469-8137.2003.00813.x

92. Hall JL (2002) Cellular mechanisms for heavy metal detoxification and tolerance. J Exp Bot 53:1–11. https://doi.org/10.1093/jexbot/53.366.1

93. Han FX, Sridhar BBM, Monts DL, Su Y (2004) Phytoavailability and toxicity of trivalent and hexavalent chromium to Brassica juncea. New Phytol 162:489–499. https://doi.org/10.1111/j.1469-8137.2004.01027.x

94. Han X, Yin H, Song X, Zhang Y, Liu M, Sang J, jiang J, Li J, Zhuo R (2016) Integration of small RNAs, degradome and transcriptome sequencing in hyperaccumulator Sedum alfredii uncovers a complex regulatory network and provides insights into cadmium phytoremediation. Plant Biotechnol J 14:1470–1483

95. Hassinen VH, Tervahauta AI, Schat H, Kärenlampi SO (2011) Plant metallothioneins-metal chelators with ROS scavenging activity? Plant Biol 13:225–232. https://doi.org/10.1111/j.1438-8677.2010.00398.x

96. Herbette S, Taconnat L, Hugouvieux V, Piette L, Magniette ML, Cuine S, Auroy P, Richaud P, Forestier C, Bourguignon J, Renou JP, Vavasseur A, Leonhardt N (2006) Genome-wide transcriptome profiling of the early cadmium response of Arabidopsis roots and shoots. Biochimie 88:1751–1765

97. Pawar, S., Ashraf, M. I., Mujawar, S., Mishra, R., and Lahiri, C. (2018). In silico identification of the indispensable quorum sensing proteins of multidrug resistant Proteus mirabilis. Front. Cell. Infect. Microbiol. 8:269. doi: 10.3389/fcimb.2018.00269

98. Chandrajit L, Pawar S, Sabarinathan R, Ashraf Md, Yamini C, Dipshikha C (2012). Identifying indispensable proteins of the type III secretion systems of Salmonella enterica serovar Typhimurium strain LT2. BMC Bioinform. 13:A10.

99. Higashimoto M, Isoyama N, Ishibashi S, Inoue M, Takiguchi M, Suzuki S, Ohnishi Y, Sato M (2009) Tissue-dependent preventive effect of metallothionein against DNA damage in dyslipidemic mice under repeated stresses of fasting or restraint. Life Sci 84:569–575

100. Hossain Z, Komatsu S (2012) Contribution of proteomic studies towards understanding plant heavy metal stress response. Front Plant Sci 3:310

101. Hossain MA, Piyatida P, Jaime A, da Silva T, Fujita M (2012a) Molecular mechanism of heavy metal toxicity and tolerance in plants: central role of glutathione in detoxification of reactive oxygen species and methylglyoxal and in heavy metal chelation. J Bot. https://doi.org/10.1155/2012/872875

102. Hossain Z, Hajika M, Komatsu S (2012b) Comparative proteome analysis of high and low cadmium accumulating soybeans under cadmium stress. Amino Acids 43:2393–2416

103. Jin S, Cheng Y, Guan Q, Liu D, Takano T, Liu S (2006). A metallothionein-like protein of rice (rgMT) functions in E. coli and its gene expression is induced by abiotic stresses. Biotechnol Lett 28:1749–1753

104. Pawar S, Davis CD, Rinehart CA (2011) Statistical analysis of microarray gene expression data from a mouse model of toxoplasmosis. BMC Bioinform 12(Suppl 7):A19

105. Mujawar, S., Mishra, R., Pawar, S., Gatherer, D., Lahiri, C.: Delineating the plausible molecular vaccine candidates and drug targets of multidrug-resistant acinetobacter baumannii. Front. Cell. Infect. Microbiol. 9, 203 (2019)

106. John R, Ahmad P, Gadgil K, Sharma S (2009) Heavy metal toxicity: effect on plant growth, biochemical parameters and metal accumulation by Brassica juncea L. Int J Plant Prod 3:65–76

107. Karin M, Cathala G, Nguyenhuu MC (1983) Expression and regulation of a human metallothionein gene carried on an autonomously replicating shuttle vector. Proc Natl Acad Sci U S A 80:4040–4044

108. Khan MIR, Khan NA (2014) Ethylene reverses photosynthetic inhibition by nickel and zinc in mustard through changes in PS II activity, photosynthetic nitrogen use efficiency, and antioxidant metabolism. Protoplasma 251:1007–1019

109. Kieffer P, Dommes J, Hoffmann L, Hausman JF, Renaut J (2008) Quantitative changes in protein expression of cadmium exposed poplar plants. Proteomics 8:2514–2430

110. Kieffer P, Planchon S, Oufir M, Ziebel J, Dommes J, Hoffmann L (2009) Combining proteomics and metabolite analyses to unravel cadmium stress- response in poplar leaves. J Proteome Res 8:400–417

111. Klapheck S, Chrost B, Starke J, Zimmermann H (1992) γ-Glutamylcysteinylserine: a new homologue of glutathione in plants of the family Poaceae. Bot Acta 105:174–179

112. Kondo N, lsobe M, Imai K, Goto T (1985) Synthesis of metallothionein-like peptides cadystin A and B occurring in a fission yeast, and their isomers. Agric Biol Chem 49:71–83

113. Lasat MM (2002) Phytoextraction of toxic metals: a review of biological mechanisms. J Environ Qual 31:109–120

114. Pawar S., Stanam A. (2019) Developing a DEVS-JAVA Model to Simulate and Pre-test Changes to Emergency Care Delivery in a Safe and Efficient Manner. In: Rojas I., Valenzuela O., Rojas F., Ortuño F. (eds) Bioinformatics and Biomedical Engineering. IWBBIO 2019. Lecture Notes in Computer Science, vol 11466. Springer, Cham. https://doi.org/10.1007/978-3-030-17935-9_1

114. Laureysens I, Blust R, De Temmerman L, Lemmens C, Ceulemans R (2004) Clonal variation in heavy metal accumulation and biomass production in a poplar coppice culture: I. Seasonal variation in leaf, wood and bark concentrations. Environ Pollut 131:485–494

115. Lee K, Bae DW, Kim SH, Han HJ, Liu X, Park HC, Lim CO, Lee SY, Chung WS (2010) Comparative proteomic analysis of the short-term responses of rice roots and leaves to cadmium. J Plant Physiol 167:161–168

116. Leopold I, Gunther D, Schmidt J, Neumann D (1999) Phytochelatins and heavy metal tolerance. Phytochemistry 50:1323–1328

117. Lingua G, Bona E, Todeschini V, Cattaneo C, Marsano F, Berta G, Cavaletto M (2012) Effects of heavy metal and arbuscularmycorrhiza on the leaf proteome of a selected Poplar clone: a time course analysis. PLoS One 7:e38662

118. Liu X, Wu H, Ji C, Wei L, Zhao J, Yu J (2013) An integrated proteomic and metabolomic study on the chronic effects of mercury in Suaeda salsa under an environmentally relevant salinity. PLoS One 8:e64041

119. Liu W, Xu L, Wang Y, Shen H, Zhu X, Zhang K, Chen Y, Yu R, Limera C, Liu L (2015a) Transcriptome-wide analysis of chromium-stress responsive microRNAs to explore miRNA8 mediated regulatory networks in radish (Raphanus sativus L.). Sci Rep 5:14024

120. Liu T, Zhu S, Tang Q, Tang S (2015b) Genome-wide transcriptomic profiling of ramie (Boehmeria nivea L. Gaud) in response to cadmium stress. Gene 558:131–137

121. Llamas A, Ullrich CI, Sanz A (2000) Cd2+effects on transmembrane electrical potential difference, respiration and membrane permeability of rice (Oryza sativa L.) roots. Plant Soil 219:21–28. https://doi.org/10.1023/A:1004753521646

122. Llamas A, Ullrich CI, Sanz A (2008) Ni2+ toxicity in rice: effect on membrane functionality and plant water content. Plant Physiol Biochem 46:905–910. https://doi.org/10.1016/j.plaphy.2008.05.006

123. Pawar, S. D., Freas, C., Weber, I. T., & Harrison, R. W. (2018). Analysis of drug resistance in HIV protease. BMC Bioinformatics, 19, 362. https://doi.org/10.1186/s12859-018-2331-y.

124. Mittal K, Choi DH, Klimov S, Pawar S, Kaur R, Mitra A, Gupta MV, Sams R, Cantuaria G, Rida PCG, Aneja R (2016b) Evaluation of centrosome clustering protein KIFC1 as a potential prognostic biomarker in serous ovarian adenocarcinomas. J Clin Oncol 34(15_suppl):e17083–e17083

125. Loebus J, Leitenmaier B, Meissner D, Braha B, Krauss GJ, Dobritzsch D, Freisinger E (2013) The major function of a metallothionein from the aquatic fungus Heliscus lugdunensis is cadmium detoxification. J Inorg Biochem 127:253–260

126. Nadgorska-Socha A, Kafel A, Kandziora-Ciupa M, Gospodarek J, Zawisza-Raszka A (2013) Accumulation of heavy metals and antioxidant responses in Viciafaba plants grown on monometallic contaminated soil. Environ Sci Pollut Res 20:1124–1134

127. Nahar K, Hasanuzzaman M, Alam MM, Rahmana A, Suzuki T, Fujita M (2016) Polyamine and nitric oxide crosstalk: antagonistic effects on cadmium toxicity in mung bean plants through up-regulating the metal detoxification, antioxidant defense and methylglyoxal detoxification systems. Ecotoxicol Environ Saf 126:245–255

128. Nakashima K, Ito Y, Yamaguchi-Shinozaki K (2009) Transcriptional regulatory networks in response to abiotic stresses in Arabidopsis and grasses. Plant Physiol 149:88–95

129. Nath S, Panda P, Mishra S, Dey M, Choudhury S, Sahoo L, Panda SK (2014) Arsenic stress in rice: redox consequences and regulation by iron. Plant Physiol Biochem 80:203–210

130. Nazar R, Iqbal N, Masood A, Iqbal M, Khan R, Syeed S, Khan NA (2012) Cadmium toxicity in plants and role of mineral nutrients in its alleviation. Am J Plant Sci 3:1476–1489. https://doi.org/10.4236/ajps.2012.310178

131. Pawar, S., & Batra, H. (2018). Online electronic laboratory notebook: A secured cloud storage system scripted in Hypertext Pre-processor (PHP) programming language. Journal of Engineering and Technology Research, 10(1), 1-6.

131. Oono Y, Yazawa T, Kawahara Y, Kanamori H, Kobayashi F, Sasaki H, Mori S, Wu Z, Handa H, Itoh T, Matsumoto T (2014) Genome-wide transcriptome analysis reveals that cadmium stress signaling controls the expression of genes in drought stress signal pathways in rice. PLoS One 9:e96946

132. Oono Y, Yazawa T, Kanamori H, Sasaki H, Mori S, Handa H, Matsumoto T (2016) Genome-wide transcriptome analysis of cadmium stress in rice. BioMed Res Int 2016:9739505
133. Opdenakker K, Remans T, Keunen E, Vangronsveld J, Cuypers A (2012) Exposure of Arabidopsis thaliana to Cd or Cu excess leads to oxidative stress mediated alterations in MAP Kinase transcript levels. Environ Exp Bot 83:53–61
134. Pandey S, Rai R, Rai LC (2012) Proteomics combines morphological, physiological and biochemical attributes to unravel the survival strategy of Anabaena sp. PCC7120 under arsenic stress. J Proteome 75:921–937
135. Patra M, Bhowmik N, Bandopadhyay B, Sharma A (2004) Comparison of mercury, lead and arsenic with respect to genotoxic effects on plant systems and the development of genetic tolerance. Environ Exp Bot 52:199–223
136. Perfus-Barbeoch L, Leonhardt N, Vavasseur A, Forestier C (2002) Heavy metal toxicity: cadmium permeates through calcium channels and disturbs the plant water status. Plant J 32:539–548. https://doi.org/10.1046/j.1365-313X.2002.01442.x
137. Peroza EA, Schmucki R, Guntert P, Freisinger E, Zerbe O (2009) The β-domain of wheat me tallothionein: a metal binding domain with a distinctive structure. J Mol Biol 387:207–218
138. shrikant pawar, Aditya Stanam. Predicting the prognosis for cancer patients with interleukins gene expression level [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2019; 2019 Mar 29-Apr 3; Atlanta, GA. Philadelphia (PA): AACR; Cancer Res 2019;79(13 Suppl):Abstract nr 4247.
138. Rascio N, Navari-Izzo F (2011) Heavy metal hyperaccumulating plants: how and why do they do it? and what makes them so interesting? Plant Sci 180:169–181
139. Rauser WE (1999) Structure and function of metal chelators produced by plants. The case for organic acids, amino acids, phytin and metallothioneins. Cell Biochem Biophys 31:19–48
140. Rezvani M, Zaefarian F, Miransari M, Nematzadeh GA (2012) Uptake and translocation of cadmium and nutrients by Aeluropus littoralis. Arch Agron Soil Sci 58:1413–1425. https://doi.org/10.1080/03650340.2011.591385
141. Ritter A, Ubertini M, Romac S, Gaillard F, Delage L, Mann A, Cock JM, Tonon T, Correa JA, Potin P (2010) Copper stress proteomics highlights local adaptation of two strains of the model brown alga Ectocarpussiliculosus. Proteomics 10:2074–2088
142. Robinson NJ, Urwin PE, Robinson PJ, Jackson PJ (1994) Gene expression in relation to metal toxicity and tolerance. In: Basra AS (ed) Stress-induced gene expression in plants. Harwood Academic Publisher, UK, pp 209–248
143. Rodriguez-Celma J, Rellan-Alvarez R, Abadia A, Abadia J, Lopez- Millan AF (2010) Changes induced by two levels of cadmium toxicity in the 2-DE protein profile of tomato roots. J Proteome 73:1694–1706
144. Roosens NH, Bernard C, Leplae R, Verbruggen N (2004) Evidence for copper homeostasis function of metallothionein (MT3) in the hyperaccumulator Thlaspi caerulescens. FEBS Lett 577:9–16. https://doi.org/10.1016/j.febslet.2004.08.084
145. Roosens NH, Leplae R, Bernard C, Verbruggen N (2005) Variations in plant metallothioneins: the heavy metal hyper accumulator Thlaspi caerulescens as a study case. Planta 222:716–729. https://doi.org/10.1007/s00425-005-0006-1
146. Rucinska-Sobkowiak R (2016) Water relations in plants subjected to heavy metal stresses. Acta Physiol Plant 38:257. https://doi.org/10.1007/s11738-016-2277-5
147. Rucinska-Sobkowiak R, Nowaczyk G, Krzesłowska M, Rabeda I, Jurga S (2013) Water status and water diffusion transport in lupine roots exposed to lead. Environ Exp Bot 87:100–109. https://doi.org/10.1016/j.envexpbot.2012.09.012
148. Ruttkay-Nedecky B, Nejd L, Gumulec J, Zitka O, Masarik M, Eckschlager T, Stiborova M, Adam V, Kizek R (2013) The role of metallothionein in oxidative stress. Int J Mol Sci 14:6044–6066. https://doi.org/10.3390/ijms14036044
149. Salt DE, Rauser WE (1995) Mg-ATP dependent transport of phytochelatins across the tonoplast of oat roots. Plant Physiol 107:1293–1301
150. Samson SLA, Gedamu L (1997) Molecular Analyses of Metallothionein Gene Regulation. Progress in Nucleic Acid Research and Molecular Biology 59:257–288
151. Pawar S. (2019) Web-Based Application for Accurately Classifying Cancer Type from Microarray Gene Expression Data Using a Support Vector Machine (SVM) Learning Algorithm. In: Rojas I., Valenzuela O., Rojas F., Ortuño F. (eds) Bioinformatics and Biomedical Engineering. IWBBIO 2019. Lecture Notes in Computer Science, vol 11466. Springer, Cham. https://doi.org/10.1007/978-3-030-17935-9_14
152. S. Pawar, A. Stanam and Y. Zhu, "Evaluating the computing efficiencies (specificity and sensitivity) of graphics processing unit (GPU)-accelerated DNA sequence alignment tools against central processing unit (CPU) alignment tool", J. Bioinf. Sequence Anal., vol. 9, no. 2, pp. 10-14, 2018.
153. Shrikant Pawar, Tuck Onn Liew, Aditya Stanam, Chandrajit Lahiri. Common cancer biomarkers of breast and ovarian types identified through artificial intelligence. Chemical Biology and Drug Design, 995-1004, https://doi.org/10.1111/cbdd.13672
154. Schneider T, Schellenberg M, Meyer S, Keller F, Gehrig P, Riedel K, Lee Y, Eberl L, Martinoia E (2009) Quantitative detection of changes in the leaf-mesophyll tonoplast proteome in dependency of a cadmium exposure of barley (Hordeumvulgare L.) plants. Proteomics 9:2668–2677
155. Semane B, Dupae J, Cuypers A, Noben JP, Tuomainen M, Tervahauta A, Sirpa K, Frank Van B, Karen S, Jaco V (2010) Leaf proteome responses of Arabidopsisthaliana exposed to mild cadmium stress. J Plant Physiol 167:247–254
156. Seth CS, Chaturvedi PK, Misra V (2008) The role of phytochelatins and antioxidants in tolerance to Cd accumulation in Brassica juncea L. Ecotoxicol Env Saf 71:76–85
157. Seth C, Remans T, Keunen E, Jozefczak M, Gielen H, Opdenakker K, Weyens N, Vangronsveld J, Cuypers A (2012) Phytoextraction of toxic metals: a central role for glutathione. Plant Cell Environ 35:334–346. https://doi.org/10.1111/j.1365-3040.2011.02338.x
158. Shameer K, Ambika S, Varghese SM, Karaba N, Udayakumar M, Sowdhamini R (2009) STIFDB – Arabidopsis stress-responsive transcription factor data base. Int J Plant Genomics 2009:583429

159. Sharma I (2012) Arsenic induced oxidative stress in plants. Biologia 67:447–453. https://doi.org/10.2478/s11756-012-0024-y
160. Sharma SS, Dietz KJ (2009) The relationship between metal toxicity and cellular redox imbalance. Trends Plant Sci 14:43–50
161. Sharmin SA, Alam I, Kim KH, Kim YG, Kim PJ, Bahk JD, Lee BH (2012) Chromium-induced physiological and proteomic alterations in roots of Miscanthussinensis. Plant Sci 187:113–126
162. Shen ZG, Zhao FJ, McGrath SP (1997) Uptake and transport of zinc in the hyperaccumulator Thlaspi caerulescens and the non-hyperaccumulator Thlaspi ochroleucum. Plant Cell Environ 20:898–906
163. Shiu SH, Shih MC, Li WH (2005) Transcription factor families have much higher expansion rates in plants than in animals. Plant Physiol 139:18–26
*164. Lahiri, Chandrajit * and Pawar, Shrikant and Mishra, Rohit (2019) Precision medicine and future of cancer treatment. Precision Cancer Medicine. ISSN 2617-2216*
165. Pawar, S., Stanam, A. A Six-Gene-Based Prognostic Model Predicts Survival in Head and Neck Squamous Cell Carcinoma Patients. J. Maxillofac. Oral Surg. 18, 320–327 (2019). https://doi.org/10.1007/s12663-019-01187-z
166. Pawar, S., Yao, X. & Lu, C. Spermine and oxacillin stress response on the cell wall synthesis and the global gene expression analysis in Methicillin-resistance Staphylococcus aureus. Genes Genom 41, 43–59 (2019). https://doi.org/10.1007/s13258-018-0735-8
167. Shukla D, Kesari R, Tiwari M, Dwivedi S, Tripathi RD, Nath P, Trivedi PK (2013) Expression of Ceratophyllum demersum phytochelatin synthase, CdPCS1, in Escherchia coli and 168. Arabidopsis enhances heavy metal(loid)s accumulation. Protoplasma 250:1263–1272. https://doi.org/10.1007/s00709-013-0508-9
169. Silva P, Matos M (2016) Assessment of the impact of aluminum on germination, early growth and free proline content in Lactuca sativa L. Ecotoxicol Environ Saf 131:151–156
170. Singh S, Parihar P, Singh R, Singh VP, Prasad SM (2015) Heavy metal tolerance in plants: role of transcriptomics, proteomics, metabolomics, and ionomics. Front Plant Sci 6:1143
171. Siripornadulsil S, Traina S, Verma DPS, Sayre RT (2002) Molecular mechanisms of proline-mediated tolerance to toxic heavy metal in transgenic microalgae. Plant Cell 14:2837–2847
172. Sobrino-Plata J, Ortega-Villasante C, Flores-Cáceres ML, Escobar C, Del Campo FF, Hernández LE (2009) Differential alterations of antioxidant defenses as bioindicators of mercury and cadmium toxicity in alfalfa. Chemosphere 77:946–954. https://doi.org/10.1016/j.chemosphere.2009.08.007
173. Sobrino-Plata J, Meyssen D, Cuypers A, Escobar C, Hernández LE (2014) Glutathione is a key antioxidant metabolite to cope with mercury and cadmium stress. Plant Soil 377:369–381
174. Solanki R, Dhankhar R (2011) Biochemical changes and adaptive strategies of plants under heavy metal stress. Biologia 66:195–204. https://doi.org/10.2478/s11756-011-0005-6
175. Song WY, Mendoza-Cozatl DG, Lee Y, Schroeder JI, Ahn SN, Lee H, Wicker T, Martinoia E (2014) Phytochelatin-metal(loid) transport into vacuoles shows different substrate preferences in barley and Arabidopsis. Plant Cell Environ 37:1192–1201. https://doi.org/10.1111/pce.12227
176. Srivalli S, Khanna-Chopra R (2008) Delayed wheat flag leaf senescence due to the removal of spikelets is associated with increased activities of leaf antioxidant enzymes, reduced glutathione/oxidized glutathione ratio and oxidative damage to mitochondrial proteins. Plant Physiol Biochem 47:663–670. https://doi.org/10.1016/j.plaphy.2009.03.015
177. Subashchandrabose SR, Wang L, Venkateswarlu K, Naidu R, Megharaj M (2017) Interactive effects of PAHs and heavy metal mixtures on oxidative stress in Chlorella sp. MM3 as determined by artificial neural network and genetic algorithm. Algal Res 21:203–212
178. Sun JY, Shen ZG (2007) Effects of Cd stress on photosynthetic characteristics and nutrient uptake of cabbages with different Cd-tolerance. Chin J Appl Ecol 18:2605–2610
179. Sytar O, Kumar A, Latowski D, Kuczynska P, Strzałka K, Prasad MNV (2013) Heavy metal-induced oxidative damage, defense reactions, and detoxifcation mechanisms in plants. Acta Physiol Plant 385:985–999
180. Takahashi H, Kawakatsu T, Wakasa Y, Hayashi S, Takaiwa F (2012) A rice transmembrane bZIP transcription factor, OsbZIP39, regulates the endoplasmic reticulum stress response. Plant Cell Physiol 53:144–153
181. Thangavel P, Long S, Minocha R (2007) Changes in phytochelatins and their biosynthetic intermediates in red spruce (Picea rubens Sarg.) cell suspension cultures under cadmium and zinc stress. Plant Cell Tissue Org Cult 88:201–216. https://doi.org/10.1007/s11240-006-9192-1
182. Toppi LS, Gabbrielli R (1999) Response to cadmium in higher plants. Environ Exp Bot 41:105–130
183. Usman K, Mienda BS, Idris S, Idris ZL (2015) Type-4 plant metallothioneins (MT4): an overview of Hordeum vulgare. Int J Tech Res Appl 3:269–271
184. Vaculık M, Konlechner C, Langer I, Adlassnig W, Puschenreiter M, Lux A, Hauser MT (2012) Root anatomy and element distribution vary between two Salix caprea isolates with different Cd accumulation capacities. Environ Pollut 163:117–126. https://doi.org/10.1016/j.envpol.2011.12.031
185. Vannini C, Marsoni M, Domingo G, Antognoni F, Biondi S, Bracale M (2009) Proteomic analysis of chromate-induced modifications in Pseudokirchneriellasubcapitata. Chemosphere 76:1372–1379
186. Pawar S., Stanam A., Lahiri C. (2020) Clustering Reveals Common Check-Point and Growth Factor Receptor Genes Expressed in Six Different Cancer Types. In: Rojas I., Valenzuela O., Rojas F., Herrera L., Ortuño F. (eds) Bioinformatics and

doi:10.20944/preprints202011.0297.v1

Biomedical Engineering. IWBBIO 2020. Lecture Notes in Computer Science, vol 12108. Springer, Cham. https://doi.org/10.1007/978-3-030-45385-5_52
187. Pawar, S., & Stanam, A. (2018). Software effort prediction with algorithm based frameworks. International Journal of Engineering and Computer Science, 7(09), 24206-24213. Retrieved from http://103.53.42.157/index.php/ijecs/article/view/4174
188. Vasak M, Hasler DW (2000) Metallothioneins: new functional and structural insights. Curr Opin Chem Biol 4:177–183
189. Verbruggen N, Hermans C, Schat H (2009) Molecular mechanisms of metal hyperaccumulation in plants. New Phytol 181:759–776. https://doi.org/10.1111/j.1469-8137.2008.02748.x
190. Zenk MH (1996) Heavy metal detoxification in higher plants- a review. Gene 179:21–30
191. Zhang H, Lian C, Shen Z (2009) Proteomic identification of small, copper-responsive proteins in germinating embryos of Oryzasativa. Ann Bot 103:923–930
192. Zhao L, Sun YL, Cui SX, Chen M, Yang HM, Liu HM, Chai TY, Huang F (2011) Cd induced changes in leaf proteome of the hyperaccumulator plant Phytolaccaamericana. Chemosphere 85:56–66
193. Zhou B, Yao W, Wang S, Wang X, Jiang T (2014) The metallothionein gene, TaMT3, from Tamarix androssowii confers Cd2+ tolerance in tobacco. Int J Mol Sci 15:10398–10409
194. Zimeri AM, Dhankher OP, McCaig B, Meagher RB (2005) The plant MT1 metallothioneins are stabilized by binding cadmiums and are required for cadmium tolerance and accumulation. Plant Mol Biol 58:839–855. https://doi.org/10.1007/s11103-005-8268-3