

References

- [1] <https://www.cancer.org/cancer/colon-rectal-cancer/about/key-statistics.html>, American Cancer Society, (accessed October 2, 2018).
- [2] M. Del Rio, F. Molina, C. Bascoul-Mollevi, V. Copois, F. Bibeau, P. Chalbos, C. Bareil, A. Kramar, N. Salvetat, C. Fraslou, E. Conseiller, V. Granci, B. Leblanc, B. Pau, P. Martineau, and M. Ychou. Gene expression signature in advanced colorectal cancer patients select drugs and response for the use of leucovorin, fluorouracil, and irinotecan. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 25(7):773–80, mar 2007. PMID: 17327601.
- [3] I. D. Nagtegaal and J. H. J. M. van Krieken. Colorectal cancer: Is the new era of colorectal cancer classification finally here? *Nature reviews. Gastroenterology & hepatology*, 10(7):391–3, jul 2013. PMID: 23689082.
- [4] D. J. Burgess. Gene expression: colorectal cancer classifications. *Nature reviews. Cancer*, 13(6):380–1, jun 2013. PMID: 23640209.
- [5] R. Martinez-Garcia, P. P. Lopez-Casas, D. Rico, A. Valencia, and M. Hidalgo. Colorectal cancer classification based on gene expression is not associated with FOLFIRI response. *Nature medicine*, 20(11):1230–1, nov 2014. PMID: 25375918.
- [6] A. Sadanandam, J. Gray, and D. Hanahan. Reply to Colorectal cancer classification based on gene expression is not associated with FOLFIRI response. *Nature medicine*, 20(11):1231–2, nov 2014. PMID: 25375919.
- [7] F. De Sousa E Melo, X. Wang, M. Jansen, E. Fessler, A. Trinh, L. P. M. H. de Rooij, J. H. de Jong, O. J. de Boer, R. van Leersum, M. F. Bijlsma, H. Rodermond, M. van der Heijden, C. J. M. van Noesel, J. B. Tuynman, E. Dekker, F. Markowitz, J. P. Medema, and L. Vermeulen. Poor-prognosis colon cancer is defined by a molecularly distinct subtype and develops from serrated precursor lesions. *Nature medicine*, 19(5):614–8, may 2013. PMID: 23584090.
- [8] A. Sadanandam, C. A. Lyssiotis, K. Homicsko, E. A. Collisson, W. J. Gibb, S. Wullschleger, L. C. G. Ostos, W. A. Lannon, C. Grotzinger, M. Del Rio, B. Lhermitte, A. B. Olshen, B. Wiedenmann, L. C. Cantley, J. W. Gray, and D. Hanahan. A colorectal cancer classification system that associates cellular phenotype and responses to therapy. *Nature medicine*, 19(5):619–25, may 2013. PMID: 23584089.
- [9] A. Sadanandam, X. Wang, F. de Sousa E Melo, J. W. Gray, L. Vermeulen, D. Hanahan, and J. P. Medema. Reconciliation of classification systems defining molecular subtypes of colorectal cancer: interrelationships and clinical implications. *Cell cycle (Georgetown, Tex.)*, 13(3):353–7, 2014. PMID: 24406433.
- [10] P. K. Sorger, S. R. B. Allerheiligen, D. R. Abernethy, R. B. Altman, K. L. R. Brouwer, A. Califano, Z. David, D. Argenio, R. Iyengar, W. J. Jusko, R. Lalonde, D. A. Lauffenburger, B. Shoichet, J. L. Stevens, S. Subramaniam, P. V. D. Graaf, R. Ward, P. K. Sorger, B. Ma, D. R. Abernethy, and R. B. Altman. Quantitative and Systems Pharmacology in the Post-genomic Era: New Approaches to Discovering Drugs and Understanding Therapeutic Mechanisms. *An NIH White Paper by the QSP Workshop Group*, pages 0–47, 2011.
- [11] A. M. Stern, M. E. Schurdak, I. Bahar, J. M. Berg, and D. L. Taylor. A Perspective on Implementing a Quantitative Systems Pharmacology Platform for Drug Discovery and the Advancement of Personalized Medicine. *Journal of biomolecular screening*, 21(6):521–34, jul 2016. PMID: 26962875.
- [12] K. Gadkar, D. C. Kirouac, D. E. Mager, P. H. Van Der Graaf, and S. Ramanujan. A six-stage workflow for robust application of systems pharmacology. *CPT: Pharmacometrics and Systems Pharmacology*, 5(5):235–249, 2016. PMID: 27299936.
- [13] K. Gadkar, N. Budha, A. Baruch, J. D. Davis, P. Fielder, and S. Ramanujan. A Mechanistic Systems Pharmacology Model for Prediction of LDL Cholesterol Lowering by PCSK9 Antagonism in Human Dyslipidemic Populations. *CPT: pharmacometrics & systems pharmacology*, 3(11):e149, nov 2014. PMID: 25426564.
- [14] S. Ait-Oudhia, M. A. Ovacik, and D. E. Mager. Systems pharmacology and enhanced pharmacodynamic models for understanding antibody-based drug action and toxicity. *mAbs*, 9(1):15–28, 2017. PMID: 27661132.

- [15] Y. Cheng, C. J. Thalhauser, S. Smithline, J. Pagidala, M. Miladinov, H. E. Vezina, M. Gupta, T. A. Leil, and B. J. Schmidt. QSP Toolbox: Computational Implementation of Integrated Workflow Components for Deploying Multi-Scale Mechanistic Models. *The AAPS Journal*, 19(4):1002–1016, 2017. PMID: 28540623.
- [16] D. C. Kirouac. How Do We "Validate" a QSP Model? *CPT: Pharmacometrics and Systems Pharmacology*, 7(9):547–548, 2018. PMID: 29761661.
- [17] J. Galon, A. Costes, F. Sanchez-Cabo, A. Kirilovsky, B. Mlecnik, C. Lagorce-Pagès, M. Tosolini, M. Camus, A. Berger, P. Wind, F. Zinzindohoué, P. Bruneval, P.-H. Cugnenc, Z. Trajanoski, W.-H. Fridman, and F. Pagès. Type, density, and location of immune cells within human colorectal tumors predict clinical outcome. *Science (New York, N.Y.)*, 313(5795):1960–4, sep 2006. PMID: 17008531.
- [18] M. Tosolini, A. Kirilovsky, B. Mlecnik, T. Fredriksen, S. Mauger, G. Bindea, A. Berger, P. Bruneval, W.-H. Fridman, F. Pagès, and J. Galon. Clinical impact of different classes of infiltrating T cytotoxic and helper cells (Th1, th2, treg, th17) in patients with colorectal cancer. *Cancer research*, 71(4):1263–71, feb 2011. PMID: 21303976.
- [19] M. J. Waldner, S. Foersch, and M. F. Neurath. Interleukin-6 - A Key Regulator of Colorectal Cancer Development. *International Journal of Biological Sciences*, 8(9):1248–1253, 2012. PMID: 23136553.
- [20] M. J. Waldner and M. F. Neurath. Colitis-associated cancer: The role of T cells in tumor development. *Seminars in Immunopathology*, 31(2):249–256, 2009. PMID: 19495757.
- [21] S. Grivennikov, E. Karin, J. Terzic, D. Mucida, G. Y. Yu, S. Vallabhapurapu, J. Scheller, S. Rose-John, H. Cheroutre, L. Eckmann, and M. Karin. IL-6 and Stat3 Are Required for Survival of Intestinal Epithelial Cells and Development of Colitis-Associated Cancer. *Cancer Cell*, 15(2):103–113, 2009. PMID: 19185845.
- [22] B. Ribba, H. P. Grimm, B. Agoram, M. R. Davies, K. Gadkar, S. Niederer, N. van Riel, J. Timmis, and P. H. van der Graaf. Methodologies for Quantitative Systems Pharmacology (QSP) Models: Design and Estimation. *CPT: pharmacometrics & systems pharmacology*, 6(8):496–498, 2017. PMID: 28585415.
- [23] A. M. Newman, C. L. Liu, M. R. Green, A. J. Gentles, W. Feng, Y. Xu, C. D. Hoang, M. Diehn, and A. A. Alizadeh. Robust enumeration of cell subsets from tissue expression profiles. *Nature methods*, 12(5):453–7, may 2015. PMID: 25822800.
- [24] T. Gong and J. D. Szustakowski. DeconRNASeq: a statistical framework for deconvolution of heterogeneous tissue samples based on mRNA-Seq data. *Bioinformatics (Oxford, England)*, 29(8):1083–5, apr 2013. PMID: 23428642.
- [25] Y. Senbabaoglu, R. S. Gejman, A. G. Winer, M. Liu, E. M. Van Allen, G. de Velasco, D. Miao, I. Ostrovskaya, E. Drill, A. Luna, N. Weinhold, W. Lee, B. J. Manley, D. N. Khalil, S. D. Kaffenberger, Y. Chen, L. Danilova, M. H. Voss, J. A. Coleman, P. Russo, V. E. Reuter, T. A. Chan, E. H. Cheng, D. A. Scheinberg, M. O. Li, T. K. Choueiri, J. J. Hsieh, C. Sander, and A. A. Hakimi. Tumor immune microenvironment characterization in clear cell renal cell carcinoma identifies prognostic and immunotherapeutically relevant messenger RNA signatures. *Genome biology*, 17(1):231, 2016. PMID: 27855702.
- [26] D. A. Barbie, P. Tamayo, J. S. Boehm, S. Y. Kim, S. E. Moody, I. F. Dunn, A. C. Schinzel, P. Sandy, E. Meylan, C. Scholl, S. Fröhling, E. M. Chan, M. L. Sos, K. Michel, C. Mermel, S. J. Silver, B. A. Weir, J. H. Reiling, Q. Sheng, P. B. Gupta, R. C. Wadlow, H. Le, S. Hoersch, B. S. Wittner, S. Ramaswamy, D. M. Livingston, D. M. Sabatini, M. Meyerson, R. K. Thomas, E. S. Lander, J. P. Mesirov, D. E. Root, D. G. Gilliland, T. Jacks, and W. C. Hahn. Systematic RNA interference reveals that oncogenic KRAS-driven cancers require TBK1. *Nature*, 462(7269):108–112, nov 2009.
- [27] M. Foroutan, D. D. Bhuva, R. Lyu, K. Horan, J. Cursons, and M. J. Davis. Single sample scoring of molecular phenotypes. *BMC bioinformatics*, 19(1):404, nov 2018. PMID: 30400809.
- [28] R. Luce and S. Perez. Parameter identification for an elliptic partial differential equation with distributed noisy data. *Inverse Problems*, 15(1):291–307, 1999.

- [29] I. Knowles. Parameter identification for elliptic problems. *Journal of Computational and Applied Mathematics*, 131(1-2):175–194, 2001.
- [30] G. Bal and G. Uhlmann. Reconstruction of coefficients in scalar second-order elliptic equations from knowledge of their solutions. *Communications on Pure and Applied Mathematics*, 66(10):1629–1652, 2013.
- [31] M. Annunziato and A. Borzi. A Fokker-Planck control framework for multidimensional stochastic processes. *Journal of Computational and Applied Mathematics*, 237(1):487–507, 2013.
- [32] A. Azouani and E. S. Titi. Feedback control of nonlinear dissipative systems by finite determining parameters - A reaction-diffusion paradigm. *Evolution Equations and Control Theory*, 3(4):579–594, oct 2014.
- [33] B. Deconinck, T. Trogdon, and V. Vasan. The Method of Fokas for Solving Linear Partial Differential Equations. *SIAM Review*, 56(1):159–186, jan 2014.
- [34] S. Roy, P. Chandrashekar, and A. S. V. Murthy. A variational approach to optical flow estimation of unsteady incompressible flows. *International Journal of Advances in Engineering Sciences and Applied Mathematics*, 7(3):149–167, 2015.
- [35] Y. Capdeboscq and J. Fehrenbach. Imaging by Modification : Numerical Reconstruction of Local Conductivities from Corresponding power density measurements. *SIAM Journal on Imaging Sciences*, 2(4):1003–1030, 2009.
- [36] G. Bal and G. Uhlmann. Inverse diffusion theory of photoacoustics. *Inverse Problems*, 26(8):085010, aug 2010.
- [37] B. J. Adesokan, K. Knudsen, V. P. Krishnan, and S. Roy. A fully non-linear optimization approach to acousto-electric tomography. *Inverse Problems*, 34(10):aad6b1, 2018.
- [38] V. Thalhofer, M. Annunziato, and A. Borzi. Stochastic modelling and control of antibiotic subtilin production. *Journal of Mathematical Biology*, 73(3):727–749, 2016.
- [39] B. A. Crawford, C. M. Kribs-Zaleta, and G. Ambartsoumian. Invasion Speed in Cellular Automaton Models for T. cruzi Vector Migration. *Bulletin of Mathematical Biology*, 75(7):1051–1081, jul 2013. PMID: 23775044.
- [40] K. Aihara and H. Suzuki. Theory of hybrid dynamical systems and its applications to biological and medical systems. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 368(1930):4893–4914, 2010. PMID: 20921003.
- [41] J. Merger, A. Borzi, and R. Herzog. Optimal control of a system of reaction–diffusion equations modeling the wine fermentation process. *Optimal Control Applications and Methods*, 38(1):112–132, 2017.
- [42] S. Hoogendoorn and P. H.L. Bovy. Simulation of pedestrian flows by optimal control and differential games. *Optimal Control Applications and Methods*, 24(3):153–172, may 2003.
- [43] S. Roy, A. Borzi, and A. Habbal. Pedestrian motion modelled by Fokker–Planck nash games. *Royal Society Open Science*, 4(9), 2017.
- [44] S. Roy, M. Annunziato, and A. Borzi. A Fokker–Planck Feedback Control-Constrained Approach for Modelling Crowd Motion. *Journal of Computational and Theoretical Transport*, 45(6):442–458, 2016.
- [45] S. Roy and A. Borzi. Numerical Investigation of a Class of Liouville Control Problems. *Journal of Scientific Computing*, 73(1):178–202, 2017. PMID: 18215681.
- [46] S. Roy, M. Annunziato, A. Borzi, and C. Klingenberg. A Fokker–Planck approach to control collective motion. *Computational Optimization and Applications*, 69(2):423–459, 2018.
- [47] A. Schindele and A. Borzi. Proximal schemes for parabolic optimal control problems with sparsity promoting cost functionals. *International Journal of Control*, 90(11):2349–2367, 2017.
- [48] S. Roy and A. Borzi. A New Optimization Approach to Sparse Reconstruction of Log-Conductivity in Acousto-Electric Tomography. *SIAM Journal on Imaging Sciences*, 11(2):1759–1784, jan 2018.

- [49] M. Paruggia. Sensitivity Analysis in Practice: A Guide to Assessing Scientific Models. *Journal of the American Statistical Association*, 101(473):398–399, mar 2006. PMID: 25246403.
- [50] J. Helton, J. Johnson, W. Oberkampf, and C. Storlie. A sampling-based computational strategy for the representation of epistemic uncertainty in model predictions with evidence theory. *Computer Methods in Applied Mechanics and Engineering*, 196(37-40):3980–3998, aug 2007.
- [51] A. Hoare, D. G. Regan, and D. P. Wilson. Sampling and sensitivity analyses tools (SaSAT) for computational modelling. *Theoretical Biology and Medical Modelling*, 5(1):4, 2008. PMID: 18304361.
- [52] B. Gomero. Latin Hypercube Sampling and Partial Rank Correlation Coefficient Analysis Applied to an Optimal Control Problem (Master's Thesis, University of Tennessee). 2012.
- [53] S. Marino, I. B. Hogue, C. J. Ray, and D. E. Kirschner. A methodology for performing global uncertainty and sensitivity analysis in systems biology. *Journal of Theoretical Biology*, 254(1):178–196, sep 2008. PMID: 18572196.