References

- 1. Clyde A. Hutchison, III *et al.*, Design and synthesis of a minimal bacterial genome. *Science* 351,aad6253(2016).DOI:10.1126/science.aad6253
- 2. Goold, H.D., Kroukamp, H., Erpf, P.E. et al. Construction and iterative redesign of synXVI a 903 kb synthetic Saccharomyces cerevisiae chromosome. Nat Commun 16, 841 (2025). https://doi.org/10.1038/s41467-024-55318-3
- 3. Greg Schuette et al. ,ChromoGen: Diffusion model predicts single-cell chromatin conformations.Sci. Adv.11,eadr8265(2025).DOI:10.1126/sciadv.adr8265
- DaSilva LF, Senan S, Patel ZM, et al. DNA-Diffusion: Leveraging Generative Models for Controlling Chromatin Accessibility and Gene Expression via Synthetic Regulatory Elements. Preprint. bioRxiv. 2024;2024.02.01.578352. Published 2024 Feb 1. doi:10.1101/2024.02.01.578352
- 5. Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 2012 Aug 17;337(6096):816-21. doi: 10.1126/science.1225829. Epub 2012 Jun 28. PMID: 22745249; PMCID: PMC6286148.
- Zhao C, Wang Y, Nie X, et al. Evaluation of the effects of sequence length and microsatellite instability on single-guide RNA activity and specificity. Int J Biol Sci. 2019;15(12):2641-2653. Published 2019 Oct 3. doi:10.7150/ijbs.37152
- 7. Eghbalsaied, S., Lawler, C., Petersen, B. et al. CRISPR/Cas9-mediated base editors and their prospects for mitochondrial genome engineering. Gene Ther 31, 209–223 (2024). https://doi.org/10.1038/s41434-023-00434-w
- 8. Jiang, T., Henderson, J.M., Coote, K. et al. Chemical modifications of adenine base editor mRNA and guide RNA expand its application scope. Nat Commun 11, 1979 (2020). https://doi.org/10.1038/s41467-020-15892-8
- 9. Lin SW, Nguyen VQ, Lin S. Preparation of Cas9 Ribonucleoproteins for Genome Editing. Bio Protoc. 2022;12(10):e4420. Published 2022 May 20. doi:10.21769/BioProtoc.4420
- Cheng H, Zhang F, Ding Y. CRISPR/Cas9 Delivery System Engineering for Genome Editing in Therapeutic Applications. Pharmaceutics. 2021;13(10):1649. Published 2021 Oct 9. doi:10.3390/pharmaceutics13101649
- 11. Kolb HC, Finn MG, Sharpless KB. Click Chemistry: Diverse Chemical Function from a Few Good Reactions. Angew Chem Int Ed Engl. 2001;40(11):2004-2021. doi:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5
- 12. Scinto SL, Bilodeau DA, Hincapie R, et al. Bioorthogonal chemistry. Nat Rev Methods Primers. 2021;1:30. doi:10.1038/s43586-021-00028-z
- 13. Mitry, M. M., Greco, F., & Osborn, H. M. (2023). In vivo applications of bioorthogonal reactions: chemistry and targeting mechanisms. Chemistry–A European Journal, 29(20), e202203942.
- 14. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell. 2006;126(4):663-676. doi:10.1016/j.cell.2006.07.024

Resources

- nature.com/subjects: biochemistry, biomaterials, biological-physics, biophysical-models, nanoscale-biophysics, biotechnology, synthetic-biology, cellular-neuroscience, neural-circuit, network-models, neurology, neuronal-development
- nature.com: Communications Biology, Neuroscience, Signal Transduction and Targeted
 Therapy

Additional References

- 1. Ponce-Alvarez, A., Deco, G. The Hopf whole-brain model and its linear approximation. Sci Rep 14, 2615 (2024). https://doi.org/10.1038/s41598-024-53105-0
- 2. Herculano-Houzel S. The human brain in numbers: a linearly scaled-up primate brain. Front Hum Neurosci. 2009;3:31. Published 2009 Nov 9. doi:10.3389/neuro.09.031.2009
- 3. Yang, Y., DeWeese, M. R., Otazu, G. H. & Zador, A. M. Millisecond-scale differences in neural activity in auditory cortex can drive decisions. Nat. Neurosci. 11, 1262–1263 (2008).
- von Bartheld CS. Myths and truths about the cellular composition of the human brain: A review of influential concepts. J Chem Neuroanat. 2018 Nov;93:2-15. doi: 10.1016/j.jchemneu.2017.08.004. Epub 2017 Sep 2. PMID: 28873338; PMCID: PMC5834348.
- 5. Kaposzta Z, Stylianou O, Mukli P, Eke A, Racz FS. Decreased connection density and modularity of functional brain networks during n-back working memory paradigm. Brain Behav. 2021;11(1):e01932. doi:10.1002/brb3.1932
- 6. Tomasi D, Volkow ND. Functional connectivity density mapping. Proc Natl Acad Sci U S A. 2010;107(21):9885-9890. doi:10.1073/pnas.1001414107
- 7. Cooray GK, Cooray V, Friston K. A cortical field theory dynamics and symmetries. J Comput Neurosci. 2024;52(4):267-284. doi:10.1007/s10827-024-00878-y
- 8. Rădulescu, A., Herron, J., Kennedy, C. et al. Global and local excitation and inhibition shape the dynamics of the cortico-striatal-thalamo-cortical pathway. Sci Rep 7, 7608 (2017). https://doi.org/10.1038/s41598-017-07527-8
- 9. Rueda-Castro V, Azofeifa JD, Chacon J, Caratozzolo P. Bridging minds and machines in Industry 5.0: neurobiological approach. Front Hum Neurosci. 2024;18:1427512. Published 2024 Aug 27. doi:10.3389/fnhum.2024.1427512
- Vaz AP, Wittig JH Jr, Inati SK, Zaghloul KA. Replay of cortical spiking sequences during human memory retrieval. Science. 2020;367(6482):1131-1134. doi:10.1126/science.aba0672
- 11. R.B. Yaffe, M.S.D. Kerr, S. Damera, S.V. Sarma, S.K. Inati, K.A. Zaghloul, Reinstatement of distributed cortical oscillations occurs with precise spatiotemporal dynamics during

- successful memory retrieval, Proc. Natl. Acad. Sci. U.S.A. 111 (52) 18727-18732, https://doi.org/10.1073/pnas.1417017112 (2014).
- 12. Yaffe, R. B., Shaikhouni, A., Arai, J., Inati, S. K., & Zaghloul, K. A. (2017). Cued Memory Retrieval Exhibits Reinstatement of High Gamma Power on a Faster Timescale in the Left Temporal Lobe and Prefrontal Cortex. The Journal of neuroscience: the official journal of the Society for Neuroscience, 37(17), 4472–4480.
- 13. Davidson, T. J., Kloosterman, F., & Wilson, M. A. (2009). Hippocampal replay of extended experience. Neuron, 63(4), 497–507. https://doi.org/10.1016/j.neuron.2009.07.027
- Huelin Gorriz, M., Takigawa, M. & Bendor, D. The role of experience in prioritizing hippocampal replay. Nat Commun 14, 8157 (2023). https://doi.org/10.1038/s41467-023-43939-z
- 15. Graham Findlay, Giulio Tononi, Chiara Cirelli, The evolving view of replay and its functions in wake and sleep, SLEEP Advances, Volume 1, Issue 1, 2020, zpab002, https://doi.org/10.1093/sleepadvances/zpab002
- Le Duigou C, Simonnet J, Teleñczuk MT, Fricker D, Miles R. Recurrent synapses and circuits in the CA3 region of the hippocampus: an associative network. Front Cell Neurosci. 2014;7:262. Published 2014 Jan 8. doi:10.3389/fncel.2013.00262
- 17. Sammons RP, Vezir M, Moreno-Velasquez L, et al. Structure and function of the hippocampal CA3 module. Proc Natl Acad Sci U S A. 2024;121(6):e2312281120. doi:10.1073/pnas.2312281120
- 18. Klinshov VV, Teramae JN, Nekorkin VI, Fukai T. Dense neuron clustering explains connectivity statistics in cortical microcircuits. PLoS One. 2014;9(4):e94292. Published 2014 Apr 14. doi:10.1371/journal.pone.0094292
- 19. Udvary D, Harth P, Macke JH, et al. The impact of neuron morphology on cortical network architecture. Cell Rep. 2022;39(2):110677. doi:10.1016/j.celrep.2022.110677
- 20. Hunt, D.L., Linaro, D., Si, B. et al. A novel pyramidal cell type promotes sharp-wave synchronization in the hippocampus. Nat Neurosci 21, 985–995 (2018). https://doi.org/10.1038/s41593-018-0172-7
- Wiera G, Mozrzymas JW. Extracellular proteolysis in structural and functional plasticity of mossy fiber synapses in hippocampus. Front Cell Neurosci. 2015;9:427. Published 2015 Nov 4. doi:10.3389/fncel.2015.00427
- 22. Fujise, K., Mishra, J., Rosenfeld, M.S. et al. Synaptic vesicle characterization of iPSC-derived dopaminergic neurons provides insight into distinct secretory vesicle pools. npj Parkinsons Dis. 11, 16 (2025). https://doi.org/10.1038/s41531-024-00862-4
- 23. Lee B, White KI, Socolich M, et al. Direct visualization of electric-field-stimulated ion conduction in a potassium channel. Cell. 2025;188(1):77-88.e15. doi:10.1016/j.cell.2024.12.006
- 24. Alonso, N., Krichmar, J.L. A sparse quantized hopfield network for online-continual memory. Nat Commun 15, 3722 (2024). https://doi.org/10.1038/s41467-024-46976-4
- 25. Predictive Sequence Learning in the Hippocampal Formation. Chen Y, Zhang H, Cameron M, Sejnowski T. bioRxiv 2022.05.19.492731; doi: https://doi.org/10.1101/2022.05.19.492731

- 26. Alonso, N., Krichmar, J.L. A sparse quantized hopfield network for online-continual memory. Nat Commun 15, 3722 (2024). https://doi.org/10.1038/s41467-024-46976-4
- 27. Insel N, Takehara-Nishiuchi K. The cortical structure of consolidated memory: a hypothesis on the role of the cingulate-entorhinal cortical connection. Neurobiol Learn Mem. 2013;106:343-350. doi:10.1016/j.nlm.2013.07.019
- 28. Woolnough O, Donos C, Rollo PS, et al. Spatiotemporal dynamics of orthographic and lexical processing in the ventral visual pathway. Nat Hum Behav. 2021;5(3):389-398. doi:10.1038/s41562-020-00982-w
- 29. Kong, X., Kong, R., Orban, C. et al. Sensory-motor cortices shape functional connectivity dynamics in the human brain. Nat Commun 12, 6373 (2021). https://doi.org/10.1038/s41467-021-26704-y
- 30. Nature news | Wi-Fi for neurons: first map of wireless nerve signals unveiled in worms: https://www.nature.com/articles/d41586-023-03619-w
- 31. Insanally, M.N., Albanna, B.F., Toth, J. *et al.* Contributions of cortical neuron firing patterns, synaptic connectivity, and plasticity to task performance. *Nat Commun* 15, 6023 (2024). https://doi.org/10.1038/s41467-024-49895-6
- 32. "Human Brain cellular composition (demythed)": von Bartheld CS. Myths and truths about the cellular composition of the human brain: A review of influential concepts. J Chem Neuroanat. 2018 Nov;93:2-15. doi: 10.1016/j.jchemneu.2017.08.004. Epub 2017 Sep 2. PMID: 28873338; PMCID: PMC5834348.
- 33. "Measure the absorbance of Cas9 protein at 280 nm using a NanoDrop Lite spectrophotometer." https://pmc.ncbi.nlm.nih.gov/articles/PMC9183966/
- 34. Stanley S. <u>Biological nanoparticles and their influence on organisms</u>. Curr Opin Biotechnol. 2014 Aug;28:69-74. doi: 10.1016/j.copbio.2013.11.014. Epub 2014 Jan 8. PMID: 24832077.
 - https://www.sciencedirect.com/science/article/abs/pii/S0958166913007155
- 35. Kaposzta Z, Stylianou O, Mukli P, Eke A, Racz FS. Decreased connection density and modularity of functional brain networks during n-back working memory paradigm. Brain Behav. 2021 Jan;11(1):e01932. doi: 10.1002/brb3.1932. Epub 2020 Nov 13. PMID: 33185986; PMCID: PMC7821619.
- 36. Lynn, C.W., Holmes, C.M. & Palmer, S.E. Heavy-tailed neuronal connectivity arises from Hebbian self-organization. Nat. Phys. 20, 484–491 (2024). https://doi.org/10.1038/s41567-023-02332-9
- 37. Wheeler, M., Smith, C., Ottolini, M. et al. Genetically targeted magnetic control of the nervous system. Nat Neurosci 19, 756–761 (2016). https://doi.org/10.1038/nn.4265
- 38. Ferritin nanocages: A biological platform for drug delivery, imaging and theranostics in cancer
- 39. Recent progress in targeted delivery vectors based on biomimetic nanoparticles | Signal Transduction and Targeted Therapy, https://www.nature.com/articles/s41392-021-00631-2
- 40. Wheeler, M., Smith, C., Ottolini, M. *et al.* Genetically targeted magnetic control of the nervous system. *Nat Neurosci* 19, 756–761 (2016). https://doi.org/10.1038/nn.4265
- 41. Tomasi D, Volkow ND. Functional connectivity density mapping. *Proc Natl Acad Sci U S A*. 2010;107(21):9885-9890. doi:10.1073/pnas.1001414107

- 42. Micrometer figure: https://pubmed.ncbi.nlm.nih.gov/38723085/#&gid=article-figures&pid=figure-5-uid-4
- 43. Yang W, Yuste R. Brain maps at the nanoscale. *Nat Biotechnol*. 2019;37(4):378-380. doi:10.1038/s41587-019-0078-2
- 44. In Situ Nanoscale Redox Mapping Using Tip-Enhanced Raman Spectroscopy., Kang G, Yang M, Mattei MS, Schatz GC, Van Duyne RP., Nano Lett. 2019 Mar 13;19(3):2106-2113. doi: 10.1021/acs.nanolett.9b00313. Epub 2019 Feb 19., PMID: 30763517
- 45. Nanoscale friction and wear maps., Tambe NS, Bhushan B., Philos Trans A Math Phys Eng Sci. 2008 Apr 28;366(1869):1405-24. doi: 10.1098/rsta.2007.2165., PMID: 18156128
- 46. In situ nanoscale mapping of the chemical composition of surfaces and 3D nanostructures by photoelectron spectromicroscopy., Ratto F, Heun S, Moutanabbir O, Rosei F., Nanotechnology. 2008 Jul 2;19(26):265703. doi: 10.1088/0957-4484/19/26/265703. Epub 2008 May 20., PMID: 21828691
- 47. Global order and local disorder in brain maps., Rothschild G, Mizrahi A., Annu Rev Neurosci. 2015 Jul 8;38:247-68. doi: 10.1146/annurev-neuro-071013-014038. Epub 2015 Apr 9., PMID: 25897872 Review.
- 48. Self-organizing maps for internal representations., Ritter H., Psychol Res. 1990;52(2-3):128-36. doi: 10.1007/BF00877520., PMID: 2281125 Review.
- 49. Borah BJ, Sun CK. A rapid denoised contrast enhancement method digitally mimicking an adaptive illumination in submicron-resolution neuronal imaging. *iScience*. 2022;25(2):103773. Published 2022 Jan 15. doi:10.1016/j.isci.2022.103773
- 50. Hancock, F., Rosas, F.E., Luppi, A.I. *et al.* Metastability demystified the foundational past, the pragmatic present and the promising future. *Nat. Rev. Neurosci.* 26, 82–100 (2025). https://doi.org/10.1038/s41583-024-00883-1
- 51. Liu, J., Jiang, C., Yu, Q. *et al.* Multidimensional free shape-morphing flexible neuromorphic devices with regulation at arbitrary points. *Nat Commun* 16, 756 (2025). https://doi.org/10.1038/s41467-024-55670-4
- 52. Paquola, C., Garber, M., Frässle, S. et al. The architecture of the human default mode network explored through cytoarchitecture, wiring and signal flow. Nat Neurosci (2025). https://doi.org/10.1038/s41593-024-01868-0