

Assignment 2 :Related work

- scientist Leonard M. Adleman launched the research field of DNA computing with a demonstration that used DNA molecules to solve a directed Hamiltonian path problem (HPP).
▼ Reference: L. M. Adleman, Science, 1994, 266, 1021–1024.
- Hsieh et al. had also demonstrated the DNA-based graph encoding computation, such as the HPP, from a theoretical perspective.
▼ Reference: S. Y. Hsieh, C. W. Huang and H. H. Chou, Appl. Math. Comput., 2008, 203, 502–512.
- several mathematical models were implemented using DNA or RNA molecules,3–9
▼ Reference:3 R. J. Lipton, Science, 1995, 268, 542–545....., D. Faulhammer, A. R. Cukras, R. J. Lipton and L. F. Landweber, Proc. Natl. Acad. Sci. U. S. A., 2000, 97, 1385–1389, 5 Y. Benenson, T. Paz-Elizur, R. Adar, E. Keinan, Z. Livneh and E. Shapiro, Nature, 2001, 414, 430–434, R. S. Braich, N. Chelyapov, C. Johnson, P. W. K. Rothmund and L. Adleman, Science, 2002, 296, 499–502, J. Y. Lee, S. Y. Shin, T. H. Park and B. T. Zhang, BioSystems, 2004, 78, 39–47, F. Tanaka, A. Kameda, M. Yamamoto and A. Ohuchi, Nucleic Acids Res., 2005, 33, 903–911, F. S. Xiong, D. Spetzler and W. D. Frasch, Integr. Biol., 2009,1, 275–280.
- and the research field of DNA self-assembly technology has recently expanded from mathematical computation to the development of a variety of nanoscale structures and devices.
▼ Reference: Y. Yang, R. Zhang and C. H. Fan, Trends Chem., 2020, 2, 137–147, H. Ramezani and H. Dietz, Nat. Rev. Genet., 2020, 21, 5–26.
- The conventional decoding approach is time-consuming since it requires multiple steps of biological operation, including repetitive magnetic bead experiments and graduated PCR.

- ▼ Reference: L. M. Adleman, *Science*, 1994, 266, 1021–1024.
- Answer determination has also been accomplished by DNA sequencing and multiple-gradient gel electrophoresis; these methods are also time-consuming
- ▼ Reference: J. Y. Lee, S. Y. Shin, T. H. Park and B. T. Zhang, *BioSystems*, 2004, 78, 39–47, M. Yamamoto, A. Kameda, N. Matsuura, T. Shiba, Y. Kawazoe and A. Ohuchi, *New Gener. Comput.*, 2002, 20, 251–261.
- As an alternative rapid decoding approach, DNA surface computing that utilizes DNA immobilized on a surface with simultaneous computation and purification,¹¹ and fluorescent probe-mediated RT-PCR^{12,13} have been proposed
- ▼ References: Q. H. Liu, L. M. Wang, A. G. Frutos, A. E. Condon, R. M. Corn and L. M. Smith, *Nature*, 2000, 403, 175–179, F. S. Xiong and W. D. Frasch, *Nat. Comput.*, 2011, 10, 947–959, Z. Ibrahim, J. A. Rose, A. Suyama and M. Khalid, *Nat. Comput.*, 2008, 7, 277–286.
- Nanopore technology is a promising method for the rapid and label-free detection of target molecules, and a data analysis method combining artificial intelligence has recently enhanced the research field.
- ▼ Reference: Y. L. Ying and Y. T. Long, *J. Am. Chem. Soc.*, 2019, 141, 15720–15729, S. M. Lu, Y. Y. Peng, Y. L. Ying and Y. T. Long, *Anal. Chem.*, 2020, 92, 5621–5644
- In particular, α -hemolysin (α HL), a pore-forming toxin from *Staphylococcus aureus*, is conventionally used as a biological nanopore for detecting oligonucleotides based on the size-matching between the pore and single-stranded DNA (ssDNA).
- ▼ References: L. Z. Song, M. R. Hobaugh, C. Shustak, S. Cheley, H. Bayley and J. E. Gouaux, *Science*, 1996, 274, 1859–1866, J. J. Kasianowicz, E. Brandin, D. Branton and D. W. Deamer, *Proc. Natl. Acad. Sci. U. S. A.*, 1996, 93, 13770–13773, A. Meller, L. Nivon, E. Brandin, J. Golovchenko and D. Branton, *Proc. Natl. Acad. Sci. U. S. A.*, 2000, 97, 1079–1084, A. Meller, L. Nivon and D. Branton, *Phys. Rev. Lett.*, 2001, 86, 3435–3438.

- A ssDNA can pass through the nanopore, whereas a double-stranded DNA (dsDNA) cannot pass and clogs the pore vestibule owing to the size mismatch. Because the results of DNA computation are output as DNA or RNA molecules.

▼ Reference: M. N. Stojanovic and D. Stefanovic, *Nat. Biotechnol.*, 2003, 21, 1069–1074, G. Seelig, D. Soloveichik, D. Y. Zhang and E. Winfree, *Science*, 2006, 314, 1585–1588, L. Qian, E. Winfree and J. Bruck, *Nature*, 2011, 475, 368–372, D. Y. Zhang and G. Seelig, *Nat. Chem.*, 2011, 3, 103–113, L. Qian and E. Winfree, *Science*, 2011, 332, 1196–1201.

- DNA computing and α HL nanopore technology have been integrated.^{33–38} Firstly, the rapid and label-free decoding of oligonucleotides in logic gate type DNA computation was proposed.³³

▼ Reference: H. Yasuga, R. Kawano, M. Takinoue, Y. Tsuji, T. Osaki, K. Kamiya, N. Miki and S. Takeuchi, *PLoS One*, 2016, 11, e0149667,... H. Yasuga, K. Inoue, R. Kawano, M. Takinoue, T. Osaki, K. Kamiya, N. Miki and S. Takeuchi, *PLoS One*, 2017, 12, e0180876....., M. Hiratani, M. Ohara and R. Kawano, *Anal. Chem.*, 2017, 89, 2312–2317..., M. Ohara, M. Takinoue and R. Kawano, *ACS Synth. Biol.*, 2017, 6, 1427–1432....., R. Kawano, *Biotechnol. J.*, 2018, 13, 1800091....., M. Hiratani and R. Kawano, *Anal. Chem.*, 2018, 90, 8531–8537

- The output molecules were translocated to another droplet through a nanopore, which was monitored electrically, and decoded. A logic network³⁴ and a more complex logic operation including enzymatic reactions³⁶

▼ Reference: H. Yasuga, K. Inoue, R. Kawano, M. Takinoue, T. Osaki, K. Kamiya, N. Miki and S. Takeuchi, *PLoS One*, 2017, 12, e0180876....., M. Ohara, M. Takinoue and R. Kawano, *ACS Synth. Biol.*, 2017, 6, 1427–1432.

- The output information of 0 or 1 in this logic operation was defined according to whether ssDNA or RNA was translocated through a nanopore. Following these studies, Hiratani et al. applied these methodologies to microRNA (miRNA) pattern recognition that can diagnose cancer from bodily fluid as a liquid biopsy.^{37,38}

▼ Reference: R. Kawano, *Biotechnol. J.*, 2018, 13, 1800091....., M. Hiratani and R. Kawano, *Anal. Chem.*, 2018, 90, 8531–8537.

- Bootstrapping of the data offered a significant improvement in distinguishing the patterns in cases where the raw unzipping time series data had been unable to distinguish any difference.^{38,39}
- ▼ Reference: M. Hiratani and R. Kawano, *Anal. Chem.*, 2018, 90, 8531–8537...., P. Liu and R. Kawano, *Small Methods*, 2020, 4, 2000101.