

Supplementary Information

Table S1 References for milestones in Fig. 1

milestone	Reference Title
Nucleic acids were first discovered (1869) ¹	The discovery of DNA
Neural Networks reported (1943) ²	A logical calculus of the ideas immanent in nervous activity
DNA double helix structure was elucidated (1953) ³	Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid
Artificial intelligence proposed (1956) ⁴	A proposal for the dartmouth summer research project on artificial intelligence
Perceptron proposed (1958) ⁵	The perceptron: a probabilistic model for information storage and organization in the brain
“Machine Learning” term reported (1959) ⁶	Some studies in machine learning using the game of checkers
Messenger RNA was first proposed (1961) ⁷	An unstable intermediate carrying information from genes to ribosomes for protein synthesis
k-Nearest neighbor reported (1967) ⁸	Nearest neighbor pattern classification
Backpropagation proposed (1974) ⁹	Beyond regression: new tools for prediction and analysis in the behavioral sciences
Sanger sequencing method (1977) ¹⁰	DNA sequencing with chain-terminating inhibitors
Ribozymes were discovered (1982) ¹¹	Self-splicing RNA: autoexcision and autocyclization of the ribosomal RNA intervening sequence of tetrahymena
Hopfield network reported (1982) ¹²	Neural networks and physical systems with emergent collective computational abilities
Polymerase Chain Reaction proposed(1983) ¹³	Enzymatic amplification of β -globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia
Classification and regression trees(1984) ¹⁴	<i>Classification And Regression Trees</i>
ID3 algorithm (1986) ¹⁵	Induction of decision trees
Q-learning algorithm (1989) ¹⁶	Learning from delayed rewards
Systematic Evolution of Ligands by Exponential enrichment proposed (1990) ¹⁷	In vitro selection of RNA molecules that bind specific ligands
DNA computing (1994) ¹⁸	Molecular Computation of Solutions to Combinatorial Problems
Support vector machine (1995) ¹⁹	Support-vector networks
Long short-term memory (1997) ²⁰	Long short-term memory
Convolutional neural network (1998) ²¹	Gradient-based learning applied to document recognition
DNA molecular machines(2000) ²²	A DNA-fuelled molecular machine made of DNA
Three-dimensional DNA nanostructures (2004) ²³	A 1.7-kilobase single-stranded DNA that folds into a

	nanoscale octahedron
DNA origami technology (2006) ²⁴	Folding DNA to create nanoscale shapes and patterns
Deep Belief Networks (2006) ²⁵	Reducing the dimensionality of data with neural networks
ML-aided RNA secondary structure prediction (2006) ²⁶	CONTRAFold: RNA secondary structure prediction without physics-based models
CRISPR-Cas9 gene editing tools (2012) ²⁷	A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity
ML-assisted analysis of DNA-protein specific binding (2015) ²⁸	Deconvolving the recognition of DNA shape from sequence
Transformer architecture (2017) ²⁹	Attention is all you need
ML-assisted prediction of CRISPR-Cas system activity(2018) ³⁰	Deep learning improves prediction of CRISPR-Cpf1 guide RNA activity
ML-assisted prediction of DNA base modifications (2019) ³¹	Detection of DNA base modifications by deep recurrent neural network on oxford nanopore sequencing data
ML-assisted prediction of immunostimulatory levels of SNAs (2019) ³²	Exploration of the nanomedicine-design space with high-throughput screening and machine learning
ML-assisted design of protein-coding DNA sequences(2019) ³³	Feedback GAN for DNA optimizes protein functions
GPT-3 (2020) ³⁴	Language models are few-shot learners
ML-assisted functional prediction of toehold switches(2020) ³⁵	A deep learning approach to programmable RNA switches
ML-assisted prediction of RNA three-dimensional structures (2021) ³⁶	Geometric deep learning of RNA structure
ML-assisted prediction of sequencing depth in NGS(2021) ³⁷	A deep learning model for predicting next-generation sequencing depth from DNA sequence
ML-assisted optimization of aptamer affinity (2021) ³⁸	Machine learning guided aptamer refinement and discovery
ML-assisted image similarity search in DNA data storage (2021) ³⁹	Molecular-level similarity search brings computing to DNA data storage
ML-assisted prediction of SSR rates (2022) ⁴⁰	A. Model-guided engineering of DNA sequences with predictable site-specific recombination rates
ML-assisted prediction of mRNA Stability(2022) ⁴¹	Deep learning models for predicting RNA degradation via dual crowdsourcing
ML-assisted functional optimization of nucleic acid polymers(2022) ⁴²	Generating experimentally unrelated target molecule-binding highly functionalized nucleic-acid polymers using machine learning
ML-assisted prediction of nucleoside hydrogel formation capability(2024) ⁴³	Developing a machine learning model for accurate nucleoside hydrogels prediction based on descriptors
ML-assisted prediction of three-dimensional shapes of DNA Origami structures(2024) ⁴⁴	Prediction of DNA origami shape using graph neural network
ML-assisted information retrieval from DNA data	Scalable and robust DNA-based storage via coding

storage(2025) ⁴⁵	theory and deep learning
ML-assisted design of functional RNA molecules(2025) ⁴⁶	Generative and predictive neural networks for the design of functional RNA molecules

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