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COVID-19 mRNA vaccine degradation rate prediction using artificial intelligence techniques: A narrative review

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ABSTRACT

As diseases become more common, the use of mRNA (messenger ribonucleic acid) vaccines is becoming more important. These vaccines can be developed quickly and have a low risk of side effects. However, they are sensitive to environmental conditions, which means they need careful storage and transport, creating challenges in distributing them. Testing the stability of an mRNA vaccine requires a lot of work and time, as it needs many lab tests. Artificial Intelligence (AI) offers a new solution by using the genetic information in RNA sequences to predict how quickly these vaccines might break down. This approach helps address potential shortages of vaccines by avoiding some of the challenges with vaccine distribution. The COVID-19 pandemic has greatly sped up the use of AI in this area. This change is significant because using AI to predict and improve the stability of mRNA vaccines was not well explored before the pandemic. This paper reviews recent studies that use AI to study mRNA vaccines during the COVID-19 pandemic. It points out that the main issue with these vaccines is how long they can be stored before they are no longer effective due to their sensitivity to environmental conditions. By looking at these studies, the paper not only shows how AI and vaccine research are coming together but also points out opportunities for more research. The goal of this review is to outline effective methods to improve the use of mRNA vaccines and encourage more scientific research and development in this field. This is an important step in improving how we deal with pandemics.

1. Introduction

The SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is a virus with a crown-like structure (Chowdhury and Oommen, 2020; Ke et al., 2020; Bogard et al., 2023; Gao et al., 2023; Yamada and Takaoka, 2023) that induces the disease COVID-19 that has threatened millions of lives (Abou Bakr, 2023; Dyer, 2023; Msemburi et al., 2023) since its outbreak in late 2019 (Wu et al., 2020; Wang et al., 2022; Ramalingam et al., 2023). Over time, COVID-19, like other viruses, mutates and tends to produce variants that are genetically different from each other. Each new mutant tends to be more lethal than the last. Several coronavirus variants have been discovered since the end of 2020. Some examples are the Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), Gamma (P.1), and Omicron (B.1.1.529) (Havers et al., 2022; Tofarides et al., 2022). Not only that, but variants could also further mutate to form subvariants. For example, Omicron BA.2.12.1 is one variant mutated out of Omicron BA.2. Past studies have recorded that mutations have been shown to

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accelerate the spread of coronaviruses (Hayawi et al., 2021). The emergence of mutant strains has raised public concern about the strength and effectiveness of COVID-19 vaccines against coronavirus-branching lineages.

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have classified variants of SARS-CoV-2 (alpha, beta, delta, gamma, and omicron) as variants of concern (VOC), but fortunately not as variants of high consequence (VOHC) (Dhawan et al., 2022; Marot et al., 2022; Rabaan et al., 2023). This classification shows that these variants of SARS-CoV-2 are more contagious and detrimental than SARS-CoV-2, are likely to be resistant to antiviral treatment, and may cause severe disease, but not to the extent that current vaccines could not provide protection. In a nutshell, vaccines are adequate and effective enough to protect against either SARS-CoV-2 or its variants, including alpha (α) (Chemaitelly et al., 2021; Flacco et al., 2021; Haas et al., 2021; Bernal et al., 2021; Liu et al., 2022), beta (β) (Abu-Raddad et al., 2021; Chemaitelly et al., 2021; Chung et al., 2021; Madhi et al., 2021; Shinde et al., 2021; Liu et al., 2022), delta (δ) (Bian et al., 2021; Bernal et al., 2021; Liu et al., 2022), gamma (γ) (Bian et al., 2021; Chung et al., 2021; Liu et al., 2022; Skowronski et al., 2022), and omicron (Muik et al., 2021; Wang et al., 2021; Carreño et al., 2022; Gao et al., 2022; Liu et al., 2022; Nemet et al., 2022; Tuekprakhon et al., 2022). Although a few drugs, namely Remdesivir and Actemra, have received full approval from the Food and Drug Administration (FDA), they are still outnumbered in the face of the COVID-19 outbreak. With this issue in hand, the FDA grants emergency use authorizations (EUAs), but not full approval, for some developed medications like molnupiravir (Zhang et al., 2020b; Vena et al., 2022). However, due to the grievous side effects, they could be deadly to the populace. As a solution to the COVID-19 pandemic is not yet possible with drug therapy, the scientists suggested that the focus should be on controlling the outbreak with disinfection and vaccination.

Vaccinologists have collaborated to develop several types of vaccines to control the spread of SARS-CoV-2. Examples include Pfizer-BioNTech's messenger ribonucleic acid (mRNA) and Sinovac, an inactivated virus-based vaccine (Mascellino et al., 2021). Of all available vaccines, nucleic acid vaccines, particularly mRNA vaccines, have received the most attention due to their promising efficacy and potential to provide a better guarantee of population health (Ioannou et al., 2022). As a result, mRNA vaccines are given high expectations and are widely considered in most preventive measures that involve vaccination. However, in terms of stability, mRNA could not be more torturous. Strengthening bonds between particles in mRNA vaccines to increase mRNA vaccine stability has been the greatest challenge for vaccinologists, but the efforts have yet to yield positive results. This results in an elevated level of importance for predicting the degradation rate of an mRNA vaccine. This article provides a novel contribution to summarizing the progress and drawing insights by reviewing the related works performed on predicting the degradation rate of an mRNA vaccine.

Artificial Intelligence (AI) finds application across a multitude of domains, permeating various sectors, including the biological sciences (Nikam and Gromiha, 2019; Santos et al., 2019; Štorkánová et al., 2021; Bhardwaj et al., 2022; Giridhar and Sampathila, 2022; Hassoun et al., 2021). Within the realm of medicine, AI has established itself as a valuable tool for disease detection (Baldwin et al., 2020; El-Sappagh et al., 2021). Recent studies have witnessed a growing focus on predicting both the future incidence (Alassafi et al., 2022; Almotairi et al., 2023; Majhi, 2023) and the severity (Jiang et al., 2020) of COVID-19 cases. However, merely forecasting COVID-19 case numbers is insufficient in effectively curtailing the spread of the pandemic. The scientific community is recommended to direct greater attention toward risk management and crisis mitigation. In this regard, mRNA vaccines emerge as a multifaceted solution capable of addressing these pressing needs. One critical aspect involves determining the degradation rate of mRNA vaccines to predict their shelf life, a paramount consideration particularly as the pursuit of long-lasting mRNA vaccines gains momentum. Vaccines serve not only during pandemics but also as crucial defenses against a wide array of viruses and diseases, rendering studies on vaccine degradation rates increasingly imperative; therefore, studies of vaccine degradation rates are in demand. To this end, the objective of this review paper—intended to inspire and raise public awareness of the potential use of AI in vaccine development—is believed to have a significant impact on the medical profession.

2. Shelf-lives of mRNA vaccines

The presence of an additional hydroxyl group in ribonucleic acid (RNA) molecules compared to deoxyribonucleic acid (DNA) molecules makes RNA more susceptible to hydrolysis. Fig. 1 presents the molecular structure of nucleic acids to provide better insights into comparing the structure of DNA with that of RNA. The chemical structure of RNA is a disadvantage in terms of stability, and this applies to vaccines as well. However, regarding genetic mutations that most vaccines, including DNA vaccines, can cause, RNA instability is less of a concern for vaccinologists. mRNA vaccines are very sensitive. Even small changes in environmental conditions can affect their half-life. Exposure to improper conditions will significantly reduce the vaccine's half-life, and it is impossible to restore the half-life or shelf-life once reduced.

mRNA is one of the three main types of single-stranded RNA that act as a messenger in all organisms, carrying genetic instructions for protein synthesis from DNA. In mRNA vaccine production, the mRNA provides information that corresponds to

a viral protein, enhancing the organism's immunity to diseases. Therefore, the degradation rate of mRNA vaccines depends on the fragility of the RNA structure used in their development. In summary, the more stable the RNA, the slower the degradation rate of the mRNA vaccine.

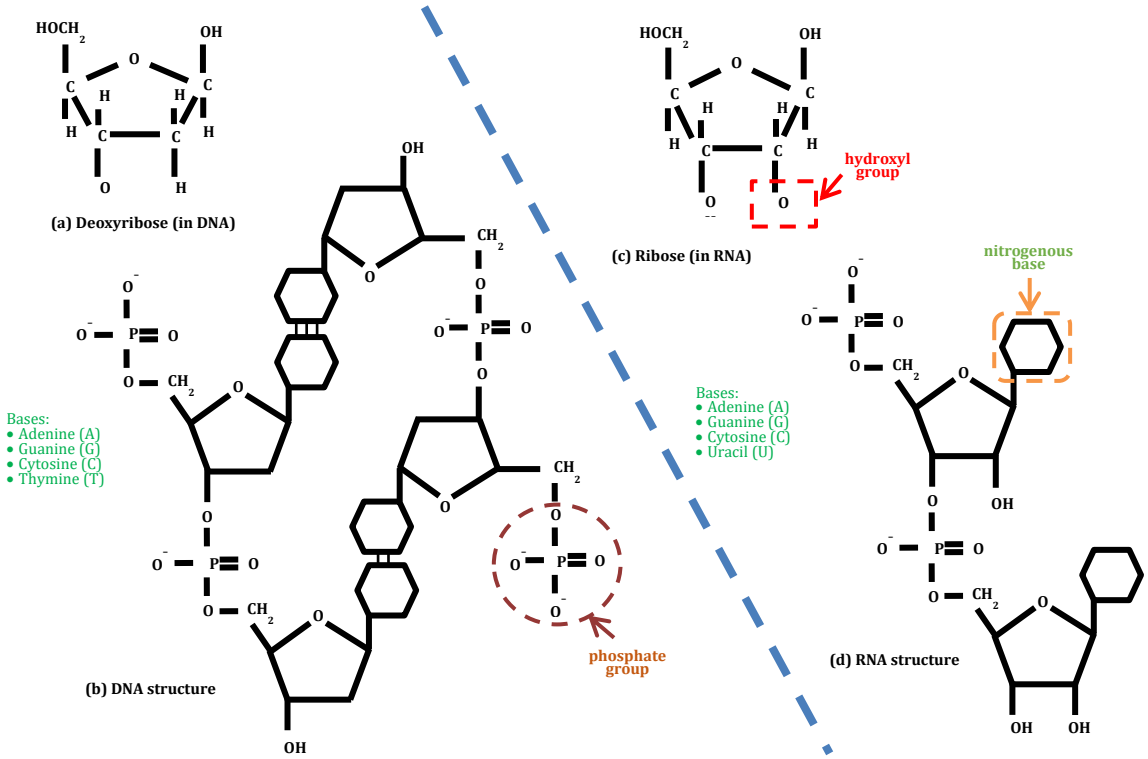

Fig. 1: Molecular structures of nucleic acids. (a) A molecular structure of the pentose sugar (deoxyribose) in DNA; (b) A molecular structure of the double-stranded helix DNA polynucleotide chain; (c) A molecular structure of the pentose sugar (ribose) in RNA; (d) A molecular structure of the single-stranded RNA polynucleotide chain

Table 1 presents the shelf-lives of some commonly used mRNA vaccines for COVID-19, providing insight into the durability of immunity of mRNA vaccines as a result of environmental conditions (Crommelin et al., 2021; Grau et al., 2021; Uddin and Roni, 2021).

Table 1: Estimated COVID-19 mRNA vaccine shelf life under example-stimulated conditions (Crommelin et al., 2021; Grau et al., 2021; Uddin and Roni, 2021)

mRNA vaccine	pH	Temperature (°C)	Shelf life
CureVac	No Data	≤ -60 (Frozen state)	3 months
		2-8	3 months
		25	24 hours
Moderna	7-8	-20 (Frozen state)	6 months
		2-8	30 days
		25	12 hours
Pfizer-BioNTech	7-8	-80 to -60 (Frozen state)	6 months
		2-8	5 days
		25	2 hours

It is observable that, with a change in temperature during vaccine shipment or storage, the shelf life of an mRNA vaccine could have been drastically reduced from months to hours. On the other hand, Table 2 provides a general overview of the RNA degradation rate by summarizing the experimental results on the half-lives of an RNA under different conditions conducted by Li and Breaker (1999) and also by Wayment-Steele et al. (2021).

Table 2: RNA half-life under example-stimulated conditions (Wayment-Steele et al., 2021)

Condition	Temperature (°C)	pH	Mg^{2+} concentration (millimolar, mM)	Half-life
Cold-chain	5	7.4	0	2.5 years
pKa shift	5	9.4	0	10 days
Room temperature*	25	7.4	0	5 days
Presence of magnesium ion (Mg^{2+})	25	7.4	14	2.016 hours

*: Standard temperature defined by International Union of Pure and Applied Chemistry (IUPAC) (Giełzak et al., 2023; Kim et al., 2023)

A vaccine could save billions through its protective immune response, but at the same time, it could kill lives with its instability. According to the statistical results presented by Dumpa et al. (2019), millions were sacrificed due to the alterations in the potency of a vaccine resulting from its unstable characteristic, therefore amplifying the importance of degradation rate prediction. Prediction allows the

estimation of the shelf life of a vaccine's immunity. Therefore, to safeguard the population from the negative impacts of vaccination and to prevent the development of social turbulence, it is necessary to update the present stage of experiments on predicting the degradation rate of an mRNA vaccine and explore the breakthrough point for improvement.

As noted above, the prediction of the rate of degradation of vaccines is of great importance, but it was not until the paroxysmal outbreak of COVID-19 in 2019 that it was given much attention. For this reason, the records on predicting vaccines' degradation rate with data analysis are only a handful, and what is more, the accessible records are limited to only COVID-19 mRNA vaccines.

3. Properties of the dataset

A key driver of this predictive research is the RNA dataset (Wayment-Steele et al., 2021) for degradation rate prediction, which Wayment-Steele et al. (2021) launched. The data set will allow researchers to predict the degradation rate for RNA used in mRNA vaccine production and test that rate under different conditions.

The database released (Wayment-Steele et al., 2021) comprises training and testing sets of 2400 and 3634 samples, respectively. The sequence, structure, and predicted_loop_type were prepared in both sets as input fields to determine the reactivity and degradation rates of the RNA sequences under different storage conditions, also known as output fields. The main features of the data set are summarized in Table 3. In addition to the two sets of data, Wayment-Steele et al. (2021) also released a matrixed form of data that delivers the probabilities of each nucleotide of every sample in both the training and testing sets being paired with adjoined nucleotides along the RNA sequence. This additional set of matrixed form data is named BPPs data, which stands for Base-pairing Probabilities (Arshadi et al., 2020). This data set has been used by some researchers (Ing et al., 2021a; 2021b; Qaid et al., 2021; Wang, 2021) to provide richer insights into their developed models for better predictive performance.

Table 3: Input and output fields of RNA datasets for the manufacturing of the COVID-19 mRNA vaccine (Wayment-Steele et al., 2021)

Feature	Field	Length	Sample	Description
Sequence	Input	107 or 130	GGAAACGUGU ...	The amino acid sequence of the mRNA vaccine candidate. This sequence determines the structure and properties of the RNA molecule and, ultimately, its potential effectiveness as a vaccine
Structure	Input	107 or 130	..(.)((...). ...	The secondary structure of the RNA molecule of the mRNA vaccine. This structure affects the interaction of RNA molecules with other molecules, including ribosomes and immune cells, and plays a role in its stability and function
Predicted_loop_type	Input	107 or 130	MMSBSSSIIISX ...	The predicted base-pairing RNA (bpRNA) loop type within the RNA molecule corresponds to the structural configuration, impacting interactions with other molecules and contributing to the overall stability of the RNA
Reactivity	Output	68 or 91	0.4368, 1.1725, ...	The measure of how readily the RNA molecule reacts with other molecules, such as ribosomes or immune cells. Higher reactivity suggests a more potent vaccine candidate, but it is also more easily degraded as it interacts more effectively with its target cells.
Deg_Mg_pH10	Output	68 or 91	0.6544, 1.0953, ...	An indication of the stability of the RNA molecule under physiological conditions. The rate at which the RNA molecule is degraded in the presence of magnesium ions (Mg^{2+}) at a pH of 10
Deg_pH10	Output	68 or 91	3.2262, 2.7048, ...	An indicator of the inherent stability of the RNA sequence itself, independent of the presence of Mg^{2+} at a pH of 10
Deg_Mg_50C	Output	68 or 91	0.2994, 0.91, ...	An indication of the stability of the RNA molecule under stress conditions, such as during storage or transportation for vaccine distribution and efficacy. The rate at which the RNA molecule is degraded in the presence of Mg^{2+} at a temperature of 50°C
Deg_50C	Output	68 or 91	0.4132, 1.1689, ...	An indicator of the inherent stability of the RNA sequence itself, independent of the presence of Mg^{2+} at 50°C

*: 'Public' sample: 107 bases (input) and 68 bases (output), 'private' sample: 130 bases (input) and 91 bases (output); Only the first 68 and 91 bases are measured because: (1) the last 39 bases are sequencer-processing and oligonucleotide-binding bases (Jolly et al., 2016; Lakhia et al., 2019; Ding et al., 2022; Kauffmann et al., 2022; Loh and Patzel, 2023); and (2) technical constraints (Wayment-Steele et al., 2021)

4. Review of related works

Since the outbreak of COVID-19 in late 2019 and the availability of data (Wayment-Steele et al., 2021), predicting the degradation rate of mRNA vaccines has been brought to attention a year later, in 2020, by Singhal (2020) and Imran et al. (2020). Following the lead of Singhal (2020) and Imran et al. (2020), the number of papers on this topic, although still limited, shows a significant increase by 2021. Practitioners have actively published their research on this prediction topic, at least tripling the number of references available by the end of 2022. Research studies published in 2023 (He et al., 2023; Vodilovska et al., 2023; Yit et al., 2023) demonstrated that active participation and engagement of researchers in this specific topic persist. All RNA sequence samples in the training set have a similar amount of nucleotides (n=107); however, that was not the case for the testing set. In the testing set, only 629 samples have 107 nucleotides; the remaining 3005 samples each have 23 additional nucleotides added to their RNA sequence. For these reasons alone, some researchers (Singhal, 2020; Wang, 2021) focused on only using the 3005 samples in the testing set for their semi-supervised prediction study.

In the fourth month of 2020, Imran et al. (2020) published a conference paper focusing solely on long short-term memory (LSTM) to study the prediction of degradation rates of RNA sequences for mRNA vaccine production with whole sets of data. Imran et al. (2020) split the training set into 1608:792 for train and valid, respectively. Different activation functions are suggested for different layers in the LSTM to ensure node preservation. As the samples in

the testing set can be categorized into two groups according to the number of bases in the RNA samples, practitioners who utilized the dataset without filtering out the minority set (which holds 107 bases) from the majority are required to test the samples separately. The minority set is known as the 'public test set,' while the majority set is known as the 'private test set' by practitioners. Accompanied by the underfitting issue, the MCRMSE (Mean Column Wise Root Mean Square Error) results scored by Imran et al. (2020) proposed LSTM model on the private and public testing sets are 0.51044 and 0.38796, respectively, averaging a score of 0.4492.

Not long after, in 2021, two more conference papers (Ing et al., 2021a; 2021b) were released exploring this topic. It is worth noting that among all the papers released, only three (Singhal, 2020; Ing et al., 2021a; 2021b) have RMSE (root mean square error) engaged in evaluating the prediction results, and two of these were the addressed conference papers published in 2021. Ing et al. (2021a) employed data sets and sizes comparable to those used by Imran et al. (2020) in semi-supervised prediction experiments. Nevertheless, Ing et al. (2021a) suggested 10-fold cross-validation rather than a percentage split. The main difference between Imran et al. (2020) and Ing et al. (2021a) is that in their conference papers, Ing et al. (2021a) focus on exploring machine learning algorithms instead of deep learning algorithms. The results of linear regression (LR) and light gradient boosting machine (LGBM) on prediction were first published by Ing et al. (2021a) before incorporating random forest (RF) (Ing et al., 2021b) into the experiment. Moreover, in the conference paper where Ing et al. (2021b) compared the results between LR, LGBM, and RF, a graphic user interface (GUI) is designed by Ing et al. (2021b) to allow interactions between users and the prediction system. GUI is a graphical user interface that entails pictographic elements, including icons, buttons, and graphs, supporting a user-system communication platform with inputs and orchestrated outputs (Martins et al., 2022; Cheng et al., 2023). In the year 2023, a well-designed web application was also devised by He et al. (2023) using the H2O Wave Python framework.

MCRMSE is a new performance metric derived from RMSE. MCRMSE is introduced along with this research topic. This performance metric is simply the average of several RMSE results, as the name suggests. As an illustration, this field of research consists of a total of five output fields ('reactivity,' 'deg_Mg_pH10,' 'deg_Mg_50C,' 'deg_pH10,' and 'deg_50C'), each of which will display its respective RMSE result after evaluation; therefore, five RMSEs are obtained. Averaging the RMSEs with the number of output fields considered (5 in this example) yields a single RMSE value equal to the single-value MCRMSE. In other words, MCRMSE assists in skipping the manual averaging procedure in research involving more than one output field. Singhal (2020) published his first findings on this topic in 2020, the same year as Asif Imran *et al.*, with three deep learning algorithms: Long short-term memory (LSTM), gated recurrent units (GRU), and graph convolution network (GCN). Singhal (2020) used all three input fields in his experiment. However, he only considered three of the five output fields. The three output fields include 'reactivity,' 'deg_Mg_pH10,' and 'deg_Mg_50C.' Furthermore, Singhal (2020) is one of the researchers who used k-fold cross-validation when splitting data in his field of study. With the approach carried out by Singhal (2020), the RMSEs of all three target outputs ('reactivity,' 'deg_Mg_pH10,' and 'deg_Mg_50C') scored by each of the algorithms manage to fall between 0.24 and 0.31.

In 2021, GCN is once again suggested for modifications by Wang (2021) and Muneer et al. (2022) to perform this prediction research. For additional information, differing from GRU and LSTM, which are classified under recurrent neural networks (RNN), GCN is an algorithm classified under artificial neural networks (ANN) (Zhang et al., 2020a). Both Wang (2021) and Muneer et al. (2022) focused on only three output fields, similar to Singhal (2020). Firstly, Wang suggests developing an improved GCN model with multi-head attention (MHA) mechanisms. She tested her modified GCN model across five folds of cross-validation. She obtained MCRMSE values of 0.3593 for 1-fold and 0.3524 for 5-fold and deduced that the error could be reduced with an increase in the number of folds for cross-validation. The prediction error was reduced by 0.0012 when Wang implemented the pseudo-label (PL) technique during modeling. In addition, Wang found that when she ensembles her improved GCN model with a WaveNet-GRU-LSTM model, a value of 0.3489 MCRMSE can be obtained.

Similar to Wang (2021) and Muneer et al. (2022) also practiced 5-fold cross-validation. Muneer et al. (2022) suggested hybridizing GCN with GRU and CNN (convolutional neural network), resulting in two hybrid models, i.e., GCN_GRU and GCN_CNN. Comparing the results between these two hybrid models, with GCN_GRU having lower errors, Muneer et al. (2022) deduced that in a base-wise experiment, CNN is underperforming. Notably, Muneer et al. (2022) considered both private and public test samples. They obtained a training and testing set of 2096 and 3000 samples, respectively, after filtering. The errors scored by GCN_GRU with the training technique performed by Muneer et al. (2022) are 0.22614 (public) and 0.34152 (private).

In the same year, an article on predicting the degradation rate of COVID-19 mRNA vaccines through RNA sequences was issued by Qaid et al. (2021). Instead of using the GCN algorithm, Qaid et al. (2021) tried the GRU and LSTM algorithms. Qaid et al. (2021) developed three hybrid models, each with three layers. The first model was developed with GRUs, whereas the second model was developed with LSTMs, occupying all three layers. The third hybrid model is modeled by sandwiching an LSTM between two GRU layers. According to Qaid

et al. (2021), all the algorithms are bidirectional, which is believed to have the ability to assist in error reduction (Bai et al., 2023). Moreover, besides the base encoding method, Qaid et al. (2021) suggested a codon encoding method to label-encode all the non-numerical inputs. As the name suggests, codon encoding involves labeling one codon (three bases) with one unique value. A codon is a form in which information is delivered; it can also be called a trinucleotide or genetic code (Knabel and Hargittai, 2021). In contrast to other researchers (Imran et al., 2020; Singhal, 2020; Ing et al., 2021a; 2021b; Muneer et al., 2022; Wang, 2021), Qaid et al. (2021) employed only the training set performing supervised learning research. Qaid et al. (2021), like Muneer et al. (2022) and Singhal (2020), augmented the data to address the overfitting problem. Qaid et al.'s (2021) experimental findings showed that codon encoding, although more prone to overfitting than base encoding, can further lower the MCRMSE.

An experiment to analyze the effect of hybridizing sequences on prediction performance is performed by Ing et al. (2022) on this degradation rate prediction topic. The experiment (Ing et al., 2022) can be construed as a continuation of Qaid et al.'s (2021) research. Ing et al. (2022) claimed that this idea was inspired after studying the article by Qaid et al. (2021). The experiment's final results demonstrated that it is not only the training technique that influences the performance of a hybrid model but also the hybridization sequence, thus cautioning practitioners. The recommendations of He et al. (2023) and Yit et al. (2023) have led to the inclusion of the nucleic transformer model into the scope of this prediction research in 2023. Both sets of authors concentrated their efforts on enhancing the encoder layer within the Nucleic Transformer framework. While these two papers employ a shared methodology for data filtering and splitting, there are variations in the defined hyperparameters. For instance, He et al. (2023) proposed the adoption of the Ranger optimizer, whereas Yit et al. (2023) advocated for the AdaBelief optimizer. Additionally, beyond the works published by He et al. (2023) and Yit et al. (2023), a conference paper authored by Sulayman (2023) emerged within the same timeframe. This paper revisited the use of RNN, specifically emphasizing a Bi-GRU architecture, with the embedding dimension parameter configured to a value of 200 (Sulayman, 2023).

Conversely, employing the same dataset, Krishna et al. (2022) and Vodilovska et al. (2023) conducted experiments to investigate strategies for enhancing model performance. Krishna et al. (2022) sought to identify effective embedding techniques to improve model efficiency, utilizing three distinct architectures—CNN, Bi-GRU, and Bi-LSTM—alongside three embedding methods: dna2vec, rna2vec, and lshvec. In their investigation, various hyperparameter configurations are experimented, including the batch size (scaled in multiples of 8, i.e., 8n, n ∈ {1, 2, 4, 8, 16}), learning rate (set at 1×10^{-n}, where n=1–5), the number of neural network layers (ranging from 2 to 10), and the size of hidden layers (spanning from 16 to 256 units) (Krishna et al., 2022).

In parallel, Vodilovska et al. (2023) undertook a comparative study of seven distinct hyperparameter optimizers (HPOs) to determine the most effective optimizer for the dataset in question. Graph Neural Networks (GNNs), with a specific focus on Graph Convolutional Networks (GCN) and Graph Attention Networks (GAT), are primarily employed across the exploration of the seven HPO candidates (Vodilovska et al., 2023). This methodological approach aimed to uncover the optimal hyperparameter optimizer that could significantly elevate the performance of the models on the given dataset. A more detailed summarization of the techniques performed by each researcher is outlined in Table 4.

5. Discussion and future research directions

AI's application is growing in tandem with its advancement. AI has been used to predict the number of infected cases for years, even before COVID-19. However, it was not until before COVID-19 that there were few to no articles on predicting the rate of vaccine degradation with AI. Overall, publications in these areas remain low in comparison with other areas of research. As described in the preceding section, predicting the degradation rate of vaccines could contribute to safeguarding critters' lives and offering new opportunities to the medical community and vaccine technology. This research may provide future vaccine technology with a beneficial role in the engineering of producing new vaccines, such as extracting and replicating sequences of RNA with low reactivity.

For this research topic, it is observable that it is difficult to agree on the comparability among the related works due to the conflicting nature of the three main variables that are essential in any experimental research. These results are based on the variability in the data sampling, model selection, and training techniques used by each researcher. Firstly, when the constant variable is data samples, the dependent variable is prediction errors, and the independent variable is training techniques, the prediction results of Imran et al. (2020), Ing et al. (2021a; 2021b), and the two findings (He et al., 2023; Yit et al., 2023) published in 2023 can be compared. The results after comparison display that, surprisingly, it is not impossible to surpass the performance of DL (deep learning) with ML (machine learning) algorithms.

Furthermore, in the case where the emphasis is on semi-supervised experiments, prediction error serves as the dependent variable, the training technique acts as the independent variable, and the specified deep learning (DL) algorithm remains the controlled variable, looking at long short-term memory (LSTM) as an illustrative example, the results available for comparative analysis are drawn from the works of Imran et al. (2020) and Singhal

(2020). On the other hand, Muneer et al.'s (2022) and Singhal's (2020) scores could be competitive if the GRU was the controlled variable. For both GRU and LSTM, it can be seen that Singhal's (2020) technique is significantly better than Imran et al.'s (2020) and Muneer et al.'s (2022) on this prediction topic in terms of errors obtained. To allow comparison among related studies, different example sets of experimental variables are defined and outlined in Table 5.

But if the prediction errors are the only concern, Qaid et al.'s (2021) training technique and developed models were found to be superior. In their articles, Singhal (2020), Imran et al. (2020), and Chze and Abdullah (2022) tabulated the prediction errors of their models during the training and validation phases, creating an opportunity to compare the models' prediction performances with those of other authors for a better evaluation. In addition to being less susceptible to overfitting, the training technique and models created by Qaid et al. (2021) also showed lower errors than all of Singhal's (2020), Imran et al.'s (2020), and Chze and Abdullah (2022) models. Therefore, by parity of reasoning, it is well-founded to make an educated guess that if Qaid et al.'s (2021) techniques and models are practiced on testing samples in conducting semi-supervised learning, their models will gain the upper hand.

Therefore, further improving the technique is a direction in which improvement can be made. Also, a typical issue with deep learning is that it is overly complicated. As a result, to avoid overfitting, most researchers (Singhal, 2020; Muneer et al., 2022; Qaid et al., 2021) used augmented data to increase the sample size for this research topic. Augmentation also helps expand the variability and unpredictability of sample data, ensuring better reliability of the performance of a model. It is recommended that hybridizing ML and DL be carried out to address the complexity problem since the experiments of Ing et al. (2021a; 2021b) have confirmed the potential of ML for this topic (Ing et al., 2021a; 2021b). However, as the findings of Ing et al. (2022) suggested, future work should take into account the hybridization order during modeling to fully explore the potential of a model. In addition, due to technical limitations in data sample development, the sequence length of the RNA samples is much less than the 3% RNA sequences used in mRNA vaccine production in an actual laboratory (Zhang et al., 2019). This limitation also places corresponding restrictions on the prediction. To increase the validity and reliability of results, it is therefore strongly advised to have a more comprehensive and expanded database with longer genetic code sequences. The RNA dataset (Wayment-Steele et al., 2021) utilized for mRNA vaccine degradation rate prediction is characterized by a wealth of features, including sequence, structure, and predicted_loop_type, providing a robust foundation for the exploration of various ML and DL approaches. ML models typically necessitate feature conversion into numerical formats, involving one-hot encoding for categorical features and, potentially, distance matrices or embedding vectors for others. These features fundamentally constitute the representational framework by which the model formulates predictions. DL models, such as RNNs, process sequences element by element, utilizing internal states to discern patterns. Conversely, alternative architectures like CNNs excel at capturing local sequence features without strictly adhering to sequential processing, providing a flexible option. While the transformative capabilities of Transformers in capturing long-range dependencies are indisputable, their complexity may not always be justified for vaccines' degradation rate prediction tasks. Depending on the specific prediction goal, simpler models such as LSTMs or CNNs may yield comparable performance, rendering them appealing choices for efficient analysis. Ultimately, the most effective approach hinges on a nuanced understanding of the data and the target variable, guiding the selection of the optimal model and feature engineering techniques.

Upon reviewing the literature, it is evident that overfitting remains a persistent challenge for researchers in this field of analysis for this topic, which has been present since its inception and continues to this day. This issue is well documented, with examples (Giridhar and Sampathila, 2022; Sulayman, 2023) where the challenge of overfitting is explicitly confirmed. These findings underscore the need for ongoing development and refinement of methodologies to mitigate overfitting, highlighting its prevalence and impact on the accuracy and generalizability of model predictions across research periods. These studies illustrate that despite advances in computational techniques and algorithm design, balancing model complexity and generalization to avoid overfitting remains a critical yet challenging aspect of research in this area.

However, amidst these challenges, some practitioners have made significant strides towards mitigating overfitting through innovative approaches. These efforts have been directed toward both refining the architecture of models (Ing et al., 2022; Krishna et al., 2022) and enhancing the processing of data (Vodilovska et al., 2023). These studies serve as pivotal references for researchers seeking to enhance the robustness and generalizability of their models, offering valuable insights into effective strategies not only in this field of analysis but broadly across machine learning and data analysis. A new era of efficiency and stability in vaccine logistics can be achieved by integrating AI into the degradation rate prediction of mRNA vaccines. mRNA vaccines, known for their stringent temperature requirements, can benefit from AI algorithms that predict degradation rates under various storage conditions. By accurately predicting how vaccines degrade under different storage conditions, AI enables a more sophisticated allocation of cold storage resources, minimizing losses and ensuring vaccines retain their efficacy until administration.

Table 4: Overview of related mRNA vaccine degradation rate prediction studies with AI

	Qaid et al. (2021)	Muneer et al. (2022)	Wang (2021)	Imran et al. (2020)	Singhal (2020)	Ing et al. (2021a)	Ing et al. (2021b)	Ing et al. (2022)	Chze and Abdullah (2022)	He et al. (2023)	Yit et al. (2023)
Learning paradigm†	S-DL	SS-DL	SS-DL	SS-DL	SS-DL	SS-ML	SS-ML	S-DL	S-DL	MT-DL, S-DL, SS-DL, UnS-DL	SS-DL
Data samples‡,§	2096, 4192**	TRS: 2096, TES: 3000	TRS: 1589, TES: 3005	TRS: 2400, TES: 3634	TRS: 3029, TES: 3005	TRS: 1589, TES: 3634	TRS: 1589, TES: 3634	2096, 4192*,*, 18524*,*	1587	TRS: 2400, TES: 3634	TRS: 2257, TES: 3634
Augmentation technique	ARNiE	Pseudo-labeling	N/A	N/A	ARNiE, CONTRAfold	N/A	N/A	ARNIE	N/A	N/A	N/A
BPPs Matrix fields††	Yes I: 3, O: 5	N/A I: 3, O: 3‡‡	Yes I: 3, O: 3‡	N/A I: 3, O: 5	N/A I: 3, O: 3‡	Yes I: 3, O: 5	Yes I: 3, O: 5	Yes I: 3, O: 5	Yes I: 3, O: 5	Yes I: 3, O: 3‡	Yes I: 3, O: 5
Encoding method	Base (0-13), Codon (1-434)	Base (0-13)	One-hot Encoding (OHE)	OHE	Hot Encoding	Base (sequence (0-3), structure (0-2), predicted_loop_type (0-6))	Base (Method_1: sequence (0-3), structure (0-2), predicted_loop_type (0-6), Method_2: 0-13)	Base (0-13)	Base (0-13)	N/A	N/A
Algorithm	LSTM, GRU	GCN, GRU, CNN	GCN	LSTM	LSTM, GRU, GCN	LR, LGBM	LR, LGBM, RF	LSTM, GRU	LSTM, GRU	Nucleic Transformer	Nucleic Transformer
Model	Bi-LSTM, Bi-GRU, Hybrid	GCN_GRU, GCN_CNN	GCN	LSTM	LSTM, GRU, GCN	LR, LGBM	LR, LGBM, RF	Bi-LSTM, Bi-GRU, Hybrid_1, Hybri_2, Hybrid_3	LSTM, GRU, L_GRU, G_LSTM, L_G_LSTM, G_L_GRU	RNAdegformer	Enhanced Nucleic Transformer
Modelling technique	All models are 3-layered and bidirectional	Statistical in silico mutagenesis (ICM)	Multi-head attention (MHA), Pseudo-labeling (PL)	Regularization, SpatialDropout1D	Added the 629 public test samples to the training set	Gradient-boosted decision trees (GBDT) boosting	Gradient-boosted decision trees (GBDT) boosting	Hybridizing sequence	N/A	1-D convolution and vanilla transformer encoder self-attention, leave-one-feature-out (LOFO), Biophysical models	5 nucleic transformer encoder layers, 1 sigmoid activation function between 2 linear layers
S/N data filtering§§	> 1	> 1	> 1	> 1	≥ 0	> 1	> 1	> 1	≥ 1	> 0.25 (TRS); > 1 (VS)	> 0.25 (TRS); > 1 (VS)
S/N_filter data filtering	N/A	N/A	1	1	N/A	1	1	N/A	1	N/A	N/A
Data splitting technique***	PS (90:10)	CV (k = 5)	CV (k = 5)	PS (67:33)	CV (k = 4)	CV (k = 10)	CV (k = 10)	PS (90:10)	CV (N/A)	CV (k = 10)	CV (k = 10)
Performance metric	MCRMSE	MCRMSE, AUC (Area Under the Curve)	MCRMSE	MCRMSE	RMSE, MAE (Mean Average Error)	RMSE	RMSE	MCRMSE	MCRMSE	MCRMSE	MCRMSE
Parameter/ Hyperparameter	0.5 dropout, 100 epochs,	Rectified linear unit	56 epochs, 256 batch sizes	0.5 dropout, 300 epochs, 0.001	50 epochs, adam	42 seeds, 32 num_leaves, 0.01	42 seeds, 32 num_leaves, 0.01	0.5 or 0 dropout, 100 epochs, 100	N/A	32 multihead attention, 265	AdaBelief/ RangerAdaBelief

† S = supervised learning, SS = semi-supervised learning, UnS = unsupervised learning, MT = multitasking.
‡ mRNA vaccine data generated by Wayment-Steele et al. (2021).
§ TRS = training set, TES = testing set, VS = validation set.
** Total number of samples after augmentation.
†† I = inputs, O = outputs.
‡‡ Lack of '*deg_pH10*' and '*deg_50C.*'
§§ S/N_filter denotes the passing state of each RNA sample during the filtering test determined by Wayment-Steele et al. (2021), with a value of 0 (fail) or 1 (pass).
*** PS = percentage split, CV = cross-validation.

	100 embedding dimensions, 512 hidden units, linear activation function, adam optimizer	(RELU) activation function, batch normalization		learning rate, RMSprop optimizer, 128 batch size, hyperbolic tangent (Tanh) activation function except linear for input and LeakyRELU for output	optimizer, 64 batch sizes	learning rate, 512 max_bin	learning rate, 512 max_bin, 100 n_estimators	embedding dimensions, 512 hidden units, linear activation function, adam optimizer		embedding size, 32 2D-convolutionfilter size, Ranger optimizer	optimizer, CrossEntropyLoss loss function, sigmoid normalization layer
Best model	LSTM with codon encoding	GCN_GRU	GCN_MHA_PL_ensemble with WaveNet-GRU-LSTM	LSTM	GRU	LGBM with BPPs matrix	LGBM with BPPs matrix and encoding Method_1	Among all: LSTM; among Hybrid: Hybrid_3 (Bi-GRU+Bi-GRU+Bi_LSTM)	Scores: LSTM with BPPs; least overfit: L_G_LSTM	RNAdegformer (semi-supervised)	Enhanced Nucleic Transformer (AdaBelief optimizer)
Results†††	TL = 0.109, VL = 0.125	U = 0.22614, R = 0.34152	R = 0.3489	TL = 0.4904, VL = 0.5165, U = 0.38796, R = 0.51044	GRU: TL = 0.1143, VL = 0.1787, R = 0.266; LSTM: T = 0.1089, V = 0.1758	0.24466	0.24466	4192 samples: LSTM: TL = 0.1180, VL = 0.1278; Hybrid_3: TL = 0.1257, VL = 0.1324; 18524 sample: LSTM: TL = 0.0143, VL = 0.151; Hybrid_3: TL = 0.0164, VL = 0.0175	LSTM: TL = 0.2679, VL = 0.2589; L_G_LSTM: TL = 0.2962, VL = 0.3035	U = 0.2291, R = 0.3372	U = 0.25034, R = 0.36454

Table 5: Comparison between the results of related studies according to experimental variables

Independent variable	Dependent variable	Controlled variable	Article‡‡‡	Best model
Training technique	Prediction errors	Data samples	Imran et al. (2020); Ing et al. (2021b; 2021a); Yit et al., (2023)	LGBM (Ing et al., 2021b)
Data sampling, training techniques	Prediction errors	DL algorithm, learning paradigm	Semi-supervised, LSTM: Imran et al. (2020); Singhal (2020) Semi-supervised, GRU: Muneer et al. (2022); Singhal (2020) Supervised: Chze and Abdullah (2022); Ing et al. (2022); Qaid et al. (2021)	Singhal's (2020) Singhal's (2020) LSTM (Qaid et al., 2021)
Hybridizing sequence, DL algorithms	Prediction errors	Data sampling, training techniques	Ing et al. (2022); Qaid et al. (2021)	Hybrid_3 (Ing et al., 2022)
Encoder layer, output fields, hyperparameters	Prediction errors	Algorithm (Nucleic Transformer)	He et al. (2023); Yit et al. (2023)	RNAdegformer (He et al., 2023)
Training technique, DL algorithms	Difference between prediction errors§§§	Model's structure (3-layered), learning paradigm (supervised)	Chze and Abdullah (2022); Ing et al. (2022); Qaid et al. (2021) Hybrid: Chze and Abdullah (2022); Ing et al. (2022); Qaid et al. (2021)	GRU (Qaid et al., 2021) Hybrid_1 (Ing et al., 2022)

††† TL = training loss, VL = validation loss, U = 'public test,' R = 'private test.'
‡‡‡ Research studies that meet comparability requirements.
§§§ The smaller the difference, the lesser the overfitting.

For example, vaccines identified by AI models as more robust against temperature variances can be allocated to areas with less sophisticated storage facilities. This judicious use of resources not only prevents vaccine wastage due to degradation but also expands the reach of vital immunization programs to more remote and underserved regions. Furthermore, AI predictions can revolutionize distribution strategies by optimizing vaccine delivery routes and schedules. The ability to accurately predict vaccine stability under different conditions allows for dynamic adjustments in the distribution chain, further reducing waste and maximizing public health impact. AI also plays a crucial role in improving inventory management within the vaccine supply chain. Through accurate degradation predictions, AI enables better stock rotation and management, ensuring that vaccines are used efficiently while at their highest efficacy. This reduces the risk of overstocking and vaccine expiration before use, addressing one of the key challenges in vaccine logistics. In short, the innovative use of artificial intelligence (AI) to predict the degradation rates of mRNA vaccines marks a pivotal progression within vaccine logistics. This review paper presents a narrative overview of the integration of AI into this field, along with a comparative analysis of the predictive accuracy of various AI algorithms in predicting mRNA vaccine degradation, offering critical and promising insights. Besides, this review paper clarifies the technological advancements, emphasizing the role of AI in optimizing logistical frameworks for vaccines and setting a new standard for efficiency and efficacy in public health initiatives. Last but not least, this research topic contributes to the third goal of the Sustainable Development Goals (SDGs) 2030: Good Health and Well-being (Vinuesa et al., 2020) through the advancement of vaccines, medicine, and health care by promoting well-being and safeguarding the lives of every age range. However, as vaccination is also used in agriculture and plant sciences (Nguyen et al., 2020; Stenberg et al., 2021; Ribal et al., 2022; Tiwari et al., 2022; Wagemans et al., 2022), in the long run, it is expected to cover more than SDG 3, such as SDG 8 and SDG 12. It, therefore, deserves further research and greater public attention.

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Compliance with ethical standards

Conflict of interest

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References

Abou Bakr EY (2023). The urgent literary response to the COVID-19 pandemic in David Hare's. Beni-Suef University International Journal of Humanities and Social Sciences, 5(1): 96-128. https://doi.org/10.21608/buijhs.2023.83462.1077

Abu-Raddad LJ, Chemaitelly H, and Butt AA (2021). Effectiveness of the BNT162b2 COVID-19 vaccine against the B.1.1.7 and B.1.351 variants. New England Journal of Medicine, 385(2): 187-189. https://doi.org/10.1056/NEJMc2104974 **PMid:33951357 PMCid:PMC8117967**

Alassafi MO, Jarrah M, and Alotaibi R (2022). Time series predicting of COVID-19 based on deep learning. Neurocomputing, 468: 335-344. https://doi.org/10.1016/j.neucom.2021.10.035 **PMid:34690432 PMCid:PMC8523546**

Almotairi KH, Hussein AM, Abualigah L, Abujayyab SK, Mahmoud EH, Ghanem BO, and Gandomi AH (2023). Impact of artificial intelligence on COVID-19 pandemic: A survey of image processing, tracking of disease, prediction of outcomes, and computational medicine. Big Data and Cognitive Computing, 7(1): 11. https://doi.org/10.3390/bdcc7010011

Arshadi AK, Webb J, Salem M, Cruz E, Calad-Thomson S, Ghadirian N, Collins J, Diez-Cecilia E, Kelly B, Goodarzi H, and Yuan JS (2020). Artificial intelligence for COVID-19 drug discovery and vaccine development. Frontiers in Artificial Intelligence, 3: 65. https://doi.org/10.3389/frai.2020.00065 **PMid:33733182 PMCid:PMC7861281**

Bai G, He S, Liu K, and Zhao J (2023). Bidirectional sentence ordering with interactive decoding. ACM Transactions on Asian and Low-Resource Language Information Processing, 22(2): 45. https://doi.org/10.1145/3561510

Baldwin DR, Gustafson J, Pickup L, Arteta C, Novotny P, Declerck J, Kadir T, Figueiras C, Sterba A, Exell A, and Potesil V et al. (2020). External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules. Thorax, 75(4): 306-312. https://doi.org/10.1136/thoraxjnl-2019-214104 **PMid:32139611 PMCid:PMC7231457**

Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, Stowe J, Tessier E, Groves N, Dabrera G, and Myers R et al. (2021). Effectiveness of COVID-19 vaccines against the B.1.617.2 (Delta) variant. The New England Journal of Medicine, 385: 585-94. https://doi.org/10.1056/NEJMoa2108891 **PMid:34289274 PMCid:PMC8314739**

Bhardwaj A, Kishore S, and Pandey DK (2022). Artificial intelligence in biological sciences. Life, 12(9): 1430. https://doi.org/10.3390/life12091430 **PMid:36143468 PMCid:PMC9505413**

Bian L, Gao Q, Gao F, Wang Q, He Q, Wu X, Mao Q, Xu M, and Liang Z et al. (2021). Impact of the Delta variant on vaccine efficacy and response strategies. Expert Review of Vaccines, 20(10): 1201-1209. https://doi.org/10.1080/14760584.2021.1976153 **PMid:34488546 PMCid:PMC8442750**

Bogard G, Barthelemy J, Hantute-Ghesquier A, Sencio V, Brito-Rodrigues P, Séron K, Robil C, Flourens A, Pinet F, Eberlé D and Trottein F et al. (2023). SARS-CoV-2 infection induces persistent adipose tissue damage in aged golden Syrian hamsters. Cell Death and Disease, 14: 75. https://doi.org/10.1038/s41419-023-05574-w **PMid:36725844 PMCid:PMC9891765**

Carreño JM, Alshammary H, Tcheou J, Singh G, Raskin AJ, Kawabata H, Sominsky LA, Clark JJ, Adelsberg DC, Bielak DA, and Gonzalez-Reiche AS et al. (2022). Activity of convalescent and vaccine serum against SARS-CoV-2 Omicron. Nature, 602(7898): 682-688.

https://doi.org/10.1038/d41586-021-03846-z
PMid:35016197

Chemaitelly H, Yassine HM, Benslimane FM, Al Khatib HA, Tang P, Hasan MR, Malek JA, Coyle P, Ayoub HH, Al Kanaani Z, and Al Kuwari E et al. (2021). mRNA-1273 COVID-19 vaccine effectiveness against the B.1.1.7 and B.1.351 variants and severe COVID-19 disease in Qatar. Nature Medicine, 27(9): 1614-1621.
https://doi.org/10.1038/s41591-021-01446-y
PMid:34244681

Cheng J, Zhao J, Xu W, Zhang T, Xue F, and Liu S (2023). Semantic similarity-based mobile application isomorphic graphical user interface identification. Mathematics, 11(3): 527.
https://doi.org/10.3390/math11030527

Chowdhury SD and Oommen AM (2020). Epidemiology of COVID-19. Journal of Digestive Endoscopy, 11(1): 03-07.
https://doi.org/10.1055/s-0040-1712187
PMCid:PMC7364648

Chung H, He S, Nasreen S, Sundaram ME, Buchan SA, Wilson SE, Chen B, Calzavara A, Fell DB, Austin PC, and Wilson K et al. (2021). Effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines against symptomatic SARS-CoV-2 infection and severe COVID-19 outcomes in Ontario, Canada: Test negative design study. BMJ, 374: n1943.
https://doi.org/10.1136/bmj.n1943
PMid:34417165 PMCid:PMC8377789

Chze ON and Abdullah AA (2022). COVID-19 mRNA vaccine degradation prediction by using deep learning algorithms. In the International Conference on Innovation and Intelligence for Informatics, Computing, and Technologies, IEEE, Sakheer, Bahrain: 444-450.
https://doi.org/10.1109/3ICT56508.2022.9990617

Crommelin DJ, Anchordoquy TJ, Volkin DB, Jiskoot W, and Mastrobattista E (2021). Addressing the cold reality of mRNA vaccine stability. Journal of Pharmaceutical Sciences, 110(3): 997-1001.
https://doi.org/10.1016/j.xphs.2020.12.006
PMid:33321139 PMCid:PMC7834447

Dhawan M, Saied AA, Mitra S, Alhumaydhi FA, Emran TB, and Wilairatana P (2022). Omicron variant (B.1.1.529) and its sublineages: What do we know so far amid the emergence of recombinant variants of SARS-CoV-2? Biomedicine and Pharmacotherapy, 154: 113522.
https://doi.org/10.1016/j.biopha.2022.113522
PMid:36030585 PMCid:PMC9376347

Ding F, Cocco S, Raj S, Manosas M, Nguyen TTT, Spiering MM, Bensimon D, Allemand JF, and Croquette V (2022). Displacement and dissociation of oligonucleotides during DNA hairpin closure under strain. Nucleic Acids Research, 50(21): 12082-12093.
https://doi.org/10.1093/nar/gkac1113
PMid:36478056 PMCid:PMC9757040

Dumpa N, Goel K, Guo Y, McFall H, Pillai AR, Shukla A, Repka MA, and Murthy SN (2019). Stability of vaccines. AAPS Pharmscitech, 20: 42.
https://doi.org/10.1208/s12249-018-1254-2
PMid:30610415

Dyer O (2023). COVID-19: China stops counting cases as models predict a million or more deaths. BMJ, 380: p2.
https://doi.org/10.1136/bmj.p2 **PMid:36596574**

El-Sappagh S, Alonso JM, Islam SR, Sultan AM, and Kwak KS (2021). A multilayer multimodal detection and prediction model based on explainable artificial intelligence for Alzheimer's disease. Scientific Reports, 11: 2660.
https://doi.org/10.1038/s41598-021-82098-3
PMid:33514817 PMCid:PMC7846613

Flacco ME, Soldato G, Acuti Martellucci C, Carota R, Di Luzio R, Caponetti A, and Manzoli L (2021). Interim estimates of COVID-19 vaccine effectiveness in a mass vaccination setting: Data from an Italian Province. Vaccines, 9(6): 628.
https://doi.org/10.3390/vaccines9060628
PMid:34200538 PMCid:PMC8227269

Gao X, Xia Y, Liu X, Xu Y, Lu P, Liu J, and Liang G (2023). A perspective on SARS-CoV-2 virus-like particles vaccines. International Immunopharmacology, 115: 109650.
https://doi.org/10.1016/j.intimp.2022.109650
PMid:36649673 PMCid:PMC9832101

Gao Y, Cai C, Grifoni A, Müller TR, Niessl J, Olofsson A, Humbert M, Hansson L, Österborg A, Bergman P, and Chen P et al. (2022). Ancestral SARS-CoV-2-specific T cells cross-recognize the Omicron variant. Nature Medicine, 28(3): 472-476.
https://doi.org/10.1038/s41591-022-01700-x
PMid:35042228 PMCid:PMC8938268

Giełżak J, Dejak B, Sokołowski J, and Bociong K (2023). Changes in strength parameters of composite cements as affected by storage temperature—A review of the literature. Coatings, 13(2): 244. https://doi.org/10.3390/coatings13020244

Giridhar A and Sampathila N (2022). Application of artificial intelligence to predict the degradation of potential mRNA vaccines developed to treat SARS-CoV-2. In the International Conference on Machine Learning and Big Data Analytics, Springer International Publishing, Patna, India: 85-94.
https://doi.org/10.1007/978-3-030-82469-3_8

Grau S, Ferrández O, Martín-García E, and Maldonado R (2021). Accidental interruption of the cold chain for the preservation of the Moderna COVID-19 vaccine. Vaccines, 9(5): 512.
https://doi.org/10.3390/vaccines9050512
PMid:34067511 PMCid:PMC8155917

Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M, Mircus G, Pan K, and Southern J et al. (2021). Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: An observational study using national surveillance data. The Lancet, 397(10287): 1819-1829.
https://doi.org/10.1016/S0140-6736(21)00947-8
PMid:33964222

Hassoun S, Jefferson F, Shi X, Stucky B, Wang J, and Rosa Jr E (2021). Artificial intelligence for biology. Integrative and Comparative Biology, 61(6): 2267-2275.
https://doi.org/10.1093/icb/icab188 **PMid:34448841**

Havers FP, Pham H, Taylor CA, Whitaker M, Patel K, Anglin O, Kambhampati AK, Milucky J, Zell E, Moline HL, and Chai SJ et al. (2022). COVID-19-associated hospitalizations among vaccinated and unvaccinated adults 18 years or older in 13 US States, January 2021 to April 2022. JAMA Internal Medicine, 182(10): 1071-1081.
https://doi.org/10.1001/jamainternmed.2022.4299
PMid:36074486 PMCid:PMC9459904

Hayawi K, Shahriar S, Serhani MA, Alashwal H, and Masud MM (2021). Vaccine versus variants (3Vs): Are the COVID-19 vaccines effective against the variants? A systematic review. Vaccines, 9(11): 1305.
https://doi.org/10.3390/vaccines9111305
PMid:34835238 PMCid:PMC8622454

He S, Gao B, Sabnis R, and Sun Q (2023). RNAdegformer: Accurate prediction of mRNA degradation at nucleotide resolution with deep learning. Briefings in Bioinformatics, 24(1): 1-14.
https://doi.org/10.1093/bib/bbac581
PMid:36633966 PMCid:PMC9851316

Imran SA, Islam MT, Shahnaz C, Islam MT, Imam OT, and Haque M (2020). COVID-19 mRNA vaccine degradation prediction using regularized LSTM model. In the IEEE International Women in Engineering (WIE) Conference on Electrical and Computer Engineering (WIECON-ECE), IEEE, Bhubaneswar, India: 328-331.
https://doi.org/10.1109/WIECON-ECE52138.2020.9398044

Ing SH, Abdullah AA, and Kanaya S (2021b). Development of COVID-19 mRNA vaccine degradation prediction system. In the International Conference on Innovation and Intelligence

for Informatics, Computing, and Technologies (3ICT), IEEE, Zallaq, Bahrain: 449-454. https://doi.org/10.1109/3ICT53449.2021.9582052

Ing SH, Abdullah AA, Harun NH, and Kanaya S (2021a). COVID-19 mRNA vaccine degradation prediction using LR and LGBM algorithms. Journal of Physics: Conference Series, 1997(1): 012005. https://doi.org/10.1088/1742-6596/1997/1/012005

Ing SH, Abdullah AA, Mashor MY, Mohamed-Hussein ZA, Mohamed Z, and Ang WC (2022). Exploration of hybrid deep learning algorithms for COVID-19 mRNA vaccine degradation prediction system. International Journal of Advances in Intelligent Informatics, 8(3): 404-416. https://doi.org/10.26555/ijain.v8i3.950

Ioannou GN, Locke ER, Green PK, and Berry K (2022). Comparison of Moderna versus Pfizer-BioNTech COVID-19 vaccine outcomes: A target trial emulation study in the US Veterans Affairs healthcare system. EClinicalMedicine, 45: 101326. https://doi.org/10.1016/j.eclinm.2022.101326 **PMid:35261970 PMCid:PMC8896984**

Jiang X, Coffee M, Bari A, Wang J, Jiang X, Huang J, Shi J, Dai J, Cai J, Zhang T, and Wu Z et al. (2020). Towards an artificial intelligence framework for data-driven prediction of coronavirus clinical severity. Computers, Materials and Continua, 63(1): 537-551. https://doi.org/10.32604/cmc.2020.010691

Jolly P, Estrela P, and Ladomery M (2016). Oligonucleotide-based systems: DNA, microRNAs, DNA/RNA aptamers. Essays in Biochemistry, 60(1): 27-35. https://doi.org/10.1042/EBC20150004 **PMid:27365033 PMCid:PMC4986462**

Kauffmann AD, Kennedy SD, Moss WN, Kierzek E, Kierzek R, and Turner DH (2022). Nuclear magnetic resonance reveals a two hairpin equilibrium near the 3′-splice site of influenza A segment 7 mRNA that can be shifted by oligonucleotides. RNA Society, 28(4): 508-522. https://doi.org/10.1261/rna.078951.121 **PMid:34983822 PMCid:PMC8925974**

Ke Z, Oton J, Qu K, Cortese M, Zila V, McKeane L, Nakane T, Zivanov J, Neufeldt CJ, Cerikan B, and Lu JM et al. (2020). Structures and distributions of SARS-CoV-2 spike proteins on intact virions. Nature, 588(7838): 498-502. https://doi.org/10.1038/s41586-020-2665-2 **PMid:32805734 PMCid:PMC7116492**

Kim JH, Kim SH, Kim BJ, and Lee HM (2023). Effects of oxygen-containing functional groups on the electrochemical performance of activated carbon for EDLCs. Nanomaterials, 13(2): 262. https://doi.org/10.3390/nano13020262 **PMid:36678013 PMCid:PMC9861518**

Knabel SJ and Hargittai I (2021). Paradigms and paradoxes: Decoding the "genetic code." Structural Chemistry, 32(1): 9-10. https://doi.org/10.1007/s11224-020-01653-2

Krishna UV, Premjith B, and Soman KP (2022). A comparative study of pre-trained gene embeddings for COVID-19 mRNA vaccine degradation prediction. In: Giri D, Choo KKR, Ponnusamy S, Meng W, Akleylek S, and Maity SP (Eds.), Proceedings of the seventh international conference on mathematics and computing: Advances in intelligent systems and computing: 302-308. Volume 1412, Springer, Singapore, Singapore. https://doi.org/10.1007/978-981-16-6890-6_22

Lakhia R, Mishra A, and Patel V (2019). Manipulation of renal gene expression using oligonucleotides. Methods in Cell Biology, 154: 109-120. https://doi.org/10.1016/bs.mcb.2019.05.006 **PMid:31493813 PMCid:PMC7992197**

Li Y and Breaker RR (1999). Kinetics of RNA degradation by specific base catalysis of transesterification involving the 2′-hydroxyl group. Journal of the American Chemical Society, 121(23): 5364-5372. https://doi.org/10.1021/ja990592p

Liu J, Chandrashekar A, Sellers D, Barrett J, Jacob-Dolan C, Lifton M, McMahan K, Sciacca M, VanWyk H, Wu C, and Yu J et al. (2022). Vaccines elicit highly conserved cellular immunity to SARS-CoV-2 Omicron. Nature, 603(7901): 493-496. https://doi.org/10.1038/s41586-022-04465-y **PMid:35102312 PMCid:PMC8930761**

Loh PS and Patzel V (2023). Non-covalent linkage of helper functions to dumbbell-shaped DNA vectors for targeted delivery. Pharmaceutics, 15(2): 370. https://doi.org/10.3390/pharmaceutics15020370 **PMid:36839697 PMCid:PMC9962178**

Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, Padayachee SD, Dheda K, Barnabas SL, Bhorat QE, and Briner C et al. (2021). Efficacy of the ChAdOx1 nCoV-19 COVID-19 vaccine against the B.1.351 variant. New England Journal of Medicine, 384(20): 1885-1898. https://doi.org/10.1056/NEJMoa2102214 **PMid:33725432 PMCid:PMC7993410**

Majhi B (2023). A modified artificial neural network (ANN)-based time series prediction of COVID-19 cases from multi-country data. Journal of the Institution of Engineers (India): Series B, 104(2): 335-350. https://doi.org/10.1007/s40031-022-00849-w **PMCid:PMC9841947**

Marot S, Bocar Fofana D, Flandre P, Malet I, Zafilaza K, Leducq V, Vivien D, Mrabet S, Poignon C, Calvez V, and Morand-Joubert L et al. (2022). SARS-CoV-2 neutralizing responses in various populations, at the time of SARS-CoV-2 variant virus emergence: Evaluation of two surrogate neutralization assays in front of whole virus neutralization test. Life, 12(12): 2064. https://doi.org/10.3390/life12122064 **PMid:36556429 PMCid:PMC9782962**

Martins JE, D'Alimonte D, Simões J, Sousa S, Esteves E, Rosa N, Correia MJ, Simões M, and Barros M (2022). MODeLING.Vis: A graphical user interface toolbox developed for machine learning and pattern recognition of biomolecular data. Symmetry, 15(1): 42. https://doi.org/10.3390/sym15010042

Mascellino MT, Di Timoteo F, De Angelis M, and Oliva A (2021). Overview of the main anti-SARS-CoV-2 vaccines: Mechanism of action, efficacy and safety. Infection and Drug Resistance, 14: 3459-3476. https://doi.org/10.2147/IDR.S315727 **PMid:34511939 PMCid:PMC8418359**

Msemburi W, Karlinsky A, Knutson V, Aleshin-Guendel S, Chatterji S, and Wakefield J (2023). The WHO estimates of excess mortality associated with the COVID-19 pandemic. Nature, 613(7942): 130-137. https://doi.org/10.1038/s41586-022-05522-2 **PMid:36517599 PMCid:PMC9812776**

Muik A, Wallisch AK, Sänger B, Swanson KA, Mühl J, Chen W, Cai H, Maurus D, Sarkar R, Türeci Ö, and Dormitzer PR et al. (2021). Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine–elicited human sera. Science, 371(6534): 1152-1153. https://doi.org/10.1126/science.abg6105 **PMid:33514629 PMCid:PMC7971771**

Muneer A, Fati SM, Akbar NA, Agustriawan D, and Wahyudi ST (2022). iVaccine-Deep: Prediction of COVID-19 mRNA vaccine degradation using deep learning. Journal of King Saud University-Computer and Information Sciences, 34(9): 7419-7432. https://doi.org/10.1016/j.jksuci.2021.10.001 **PMid:38620874 PMCid:PMC8513509**

Nemet I, Kliker L, Lustig Y, Zuckerman N, Erster O, Cohen C, Kreiss Y, Alroy-Preis S, Regev-Yochay G, Mendelson E, and Mandelboim M et al. (2022). Third BNT162b2 vaccination neutralization of SARS-CoV-2 Omicron infection. New England Journal of Medicine, 386(5): 492-494. https://doi.org/10.1056/NEJMc2119358 **PMid:34965337 PMCid:PMC8823651**

Nguyen NH, Trotel-Aziz P, Villaume S, Rabenoelina F, Schwarzenberg A, Nguema-Ona E, Clément C, Baillieul F, and Aziz A (2020). Bacillus subtilis and Pseudomonas fluorescens trigger common and distinct systemic immune responses in Arabidopsis thaliana depending on the pathogen lifestyle. Vaccines, 8(3): 503.
https://doi.org/10.3390/vaccines8030503
PMid:32899695 PMCid:PMC7563191

Nikam R and Gromiha MM (2019). Seq2Feature: A comprehensive web-based feature extraction tool. Bioinformatics, 35(22): 4797-4799.
https://doi.org/10.1093/bioinformatics/btz432
PMid:31135038

Qaid TS, Mazaar H, Alqahtani MS, Raweh AA, and Alakwaa W (2021). Deep sequence modelling for predicting COVID-19 mRNA vaccine degradation. PeerJ Computer Science, 7: e597.
https://doi.org/10.7717/peerj-cs.597
PMid:34239977 PMCid:PMC8237341

Rabaan AA, Al-Ahmed SH, Albayat H, Alwarthan S, Alhajri M, Najim MA, AlShehail BM, Al-Adsani W, Alghadeer A, Abduljabbar WA, and Alotaibi N et al. (2023). Variants of SARS-CoV-2: Influences on the vaccines' effectiveness and possible strategies to overcome their consequences. Medicina, 59(3): 507.
https://doi.org/10.3390/medicina59030507
PMid:36984508 PMCid:PMC10051174

Ramalingam S, Thamizhvel R, Sudagar S, and Silambarasan R (2023). Production of third generation bio-fuel through thermal cracking process by utilizing COVID-19 plastic wastes. Materials Today: Proceedings, 72: 1618-1623.
https://doi.org/10.1016/j.matpr.2022.09.430
PMid:36213622 PMCid:PMC9529355

Ribal J, Marques-Perez I, and Segura M (2022). A farm compensation model to reduce the risk of pest spreading: An application for Xylella fastidiosa in Mediterranean agriculture. NJAS: Impact in Agricultural and Life Sciences, 94(1): 112-136. https://doi.org/10.1080/27685241.2022.2108732

Santos AG, da Rocha GO, and de Andrade JB (2019). Occurrence of the potent mutagens 2-nitrobenzanthrone and 3-nitrobenzanthrone in fine airborne particles. Scientific Reports, 9: 1.
https://doi.org/10.1038/s41598-018-37186-2
PMid:30626917 PMCid:PMC6327027

Shinde V, Bhikha S, Hoosain Z, Archary M, Bhorat Q, Fairlie L, Lalloo U, Masilela MS, Moodley D, Hanley S, and Fouche L et al. (2021). Efficacy of NVX-CoV2373 COVID-19 vaccine against the B.1.351 variant. New England Journal of Medicine, 384(20): 1899-1909.
https://doi.org/10.1056/NEJMoa2103055
PMid:33951374 PMCid:PMC8091623

Singhal A (2020). Predicting hydroxyl mediated nucleophilic degradation and molecular stability of RNA sequences through the application of deep learning methods. Arxiv Preprint Arxiv:2011.05136.
https://doi.org/10.48550/arXiv.2011.05136

Skowronski DM, Setayeshgar S, Zou M, Prystajecky N, Tyson JR, Galanis E, Naus M, Patrick DM, Sbihi H, El Adam S, and Henry B et al. (2022). Single-dose mRNA vaccine effectiveness against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including alpha and gamma variants: A test-negative design in adults 70 years and older in British Columbia, Canada. Clinical Infectious Diseases, 74(7): 1158-1165.
https://doi.org/10.1093/cid/ciab616
PMid:34244723 PMCid:PMC8406884

Stenberg JA, Sundh I, Becher PG, Björkman C, Dubey M, Egan PA, Friberg H, Gil JF, Jensen DF, Jonsson M, and Karlsson M et al. (2021). When is it biological control? A framework of definitions, mechanisms, and classifications. Journal of Pest Science, 94(3): 665-676.
https://doi.org/10.1007/s10340-021-01354-7

Štorkánová H, Oreská S, Špiritović M, Heřmánková B, Bubová K, Komarc M, Pavelka K, Vencovský J, Distler JH, Šenolt L, and Bečvář R et al. (2021). Plasma Hsp90 levels in patients with systemic sclerosis and relation to lung and skin involvement: A cross-sectional and longitudinal study. Scientific Reports, 11: 1.
https://doi.org/10.1038/s41598-020-79139-8
PMid:33414495 PMCid:PMC7791137

Sulayman N (2023). Deep learning-based predictive model of mRNA vaccine deterioration: An analysis of the Stanford COVID-19 mRNA vaccine dataset. Baghdad Science Journal, 20(4(SI)): 1451-1458.
https://doi.org/10.21123/bsj.2023.8504

Tiwari M, Pati D, Mohapatra R, Sahu BB, and Singh P (2022). The impact of microbes in plant immunity and priming induced inheritance: A sustainable approach for crop protection. Plant Stress, 4: 100072.
https://doi.org/10.1016/j.stress.2022.100072

Tofarides AG, Christaki E, Milionis H, and Nikolopoulos GK (2022). Effect of vaccination against SARS-CoV-2 on long COVID-19: A narrative review. Life, 12(12): 2057.
https://doi.org/10.3390/life12122057
PMid:36556422 PMCid:PMC9785763

Tuekprakhon A, Nutalai R, Dijokaite-Guraliuc A, Zhou D, Ginn HM, Selvaraj M, Liu C, Mentzer AJ, Supasa P, Duyvesteyn HM, and Das R et al. (2022). Antibody escape of SARS-CoV-2 Omicron BA.4 and BA.5 from vaccine and BA.1 serum. Cell, 185(14): 2422-2433.
https://doi.org/10.1016/j.cell.2022.06.005
PMid:35772405 PMCid:PMC9181312

Uddin MN Roni MA (2021). Challenges of storage and stability of mRNA-based COVID-19 vaccines. Vaccines, 9(9): 1033.
https://doi.org/10.3390/vaccines9091033
PMid:34579270 PMCid:PMC8473088

Vena A, Traman L, Bavastro M, Limongelli A, Dentone C, Magnè F, Giacobbe DR, Mikulska M, Taramasso L, Di Biagio A, and Bassetti M (2022). Early clinical experience with molnupiravir for mild to moderate breakthrough COVID-19 among fully vaccinated patients at risk for disease progression. Vaccines, 10(7): 1141.
https://doi.org/10.3390/vaccines10071141
PMid:35891305 PMCid:PMC9318911

Vinuesa R, Azizpour H, Leite I, Balaam M, Dignum V, Domisch S, Felländer A, Langhans SD, Tegmark M, and Fuso Nerini F (2020). The role of artificial intelligence in achieving the sustainable development goals. Nature Communications, 11: 233.
https://doi.org/10.1038/s41467-019-14108-y
PMid:31932590 PMCid:PMC6957485

Vodilovska V, Gievska S, and Ivanoska I (2023). Hyperparameter optimization of graph neural networks for mRNA degradation prediction. In the 46th MIPRO ICT and Electronics Convention, IEEE, Opatija, Croatia: 423-428.
https://doi.org/10.23919/MIPRO57284.2023.10159737

Wagemans J, Holtappels D, Vainio E, Rabiey M, Marzachì C, Herrero S, Ravanbakhsh M, Tebbe CC, Ogliastro M, Ayllón MA, and Turina M (2022). Going viral: Virus-based biological control agents for plant protection. Annual Review of Phytopathology, 60: 21-42.
https://doi.org/10.1146/annurev-phyto-021621-114208
PMid:35300520

Wang H, Paulson KR, Pease SA, Watson S, Comfort H, Zheng P, Aravkin AY, Bisignano C, Barber RM, Alam T, and Fuller JE et al. (2022). Estimating excess mortality due to the COVID-19 pandemic: A systematic analysis of COVID-19-related mortality, 2020–21. The Lancet, 399(10334): 1513-1536.
https://doi.org/10.1016/S0140-6736(21)02796-3

Wang P, Casner RG, Nair MS, Wang M, Yu J, Cerutti G, Liu L, Kwong PD, Huang Y, Shapiro L, and Ho DD (2021). Increased resistance of SARS-CoV-2 variant P.1 to antibody neutralization. Cell Host and Microbe, 29(5): 747-751.

https://doi.org/10.1016/j.chom.2021.04.007
PMid:33887205 PMCid:PMC8053237

Wang Y (2021). Predicting the degradation of COVID-19 mRNA vaccine with graph convolutional networks. In the 6th International Conference on Machine Learning Technologies, Association for Computing Machinery, Jeju Island, Republic of Korea: 111-116. https://doi.org/10.1145/3468891.3468907

Wayment-Steele HK, Kim DS, Choe CA, Nicol JJ, Wellington-Oguri R, Watkins AM, Parra Sperberg RA, Huang PS, Participants E, and Das R (2021). Theoretical basis for stabilizing messenger RNA through secondary structure design. Nucleic Acids Research, 49(18): 10604-10617.
https://doi.org/10.1093/nar/gkab764
PMid:34520542 PMCid:PMC8499941

Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, and Yuan ML et al. (2020). A new coronavirus associated with human respiratory disease in China. Nature, 579(7798): 265-269.
https://doi.org/10.1038/s41586-020-2008-3
PMid:32015508 PMCid:PMC7094943

Yamada T and Takaoka A (2023). Innate immune recognition against SARS-CoV-2. Inflammation and Regeneration, 43: 7.
https://doi.org/10.1186/s41232-023-00259-5
PMid:36703213 PMCid:PMC9879261

Yit TW, Hassan R, Zakaria NH, Kasim S, Moi SH, Khairuddin AR, and Amnur H (2023). Transformer in mRNA degradation prediction. International Journal on Informatics Visualization, 7(2): 588-599. https://doi.org/10.30630/joiv.7.2.1165

Zhang C, Maruggi G, Shan H, and Li J (2019). Advances in mRNA vaccines for infectious diseases. Frontiers in Immunology, 10: 429065.
https://doi.org/10.3389/fimmu.2019.00594
PMid:30972078 PMCid:PMC6446947

Zhang J, Tan L, Tao X, Pham T, and Chen B (2020a). Relational intelligence recognition in online social networks: A survey. Computer Science Review, 35: 100221.
https://doi.org/10.1016/j.cosrev.2019.100221

Zhang LK, Sun Y, Zeng H, Wang Q, Jiang X, Shang WJ, Wu Y, Li S, Zhang YL, Hao ZN, and Chen H et al. (2020b). Calcium channel blocker amlodipine besylate therapy is associated with reduced case fatality rate of COVID-19 patients with hypertension. Cell Discovery, 6: 96.
https://doi.org/10.1038/s41421-020-00235-0
PMid:33349633 PMCid:PMC7752915