COVID-19 Modeling: A Review*

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Abstract

To tackle the COVID-19 pandemic, massive efforts have been made in modeling COVID-19 transmission, diagnoses, interventions, pathological and influence analysis, etc. With the most comprehensive repository on COVID-19 research - some 160k WHO-collected global literature on COVID-19 produced since 2020, some critical question to ask include: What are the COVID-19 challenges? How do they address the challenges? Where are the significant gaps and opportunities in COVID-19 modeling?. Accordingly, informed by their statistics and a deep keyword-based similarity analysis of those references on COVID-19 modeling, this is the first to systematically summarize the disease, data and modeling challenges and the corresponding modeling progress and gaps. We come up with a transdisciplinary research landscape to summarize and match the business goals and tasks and their learning methods of COVID-19 modeling.

1 Introduction

In 2020, COVID-19 modeling emerged as the most imperative yet challenging task for scientists across disciplines including medicine, health, science, computer science, and social science. Similar to the significant challenges posed by the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) virus and its COVID-19 disease to health, government, society and economy, they also introduce unique challenges and opportunities to science and research communities. One critical research task is the COVID-19 modeling, i.e., quantitatively understanding and characterizing the virus and disease characteristics and estimating and predicting COVID-19 transmission, case identification and trends, intervention measures and their effects, and their impacts on social, economic, psychological and political aspects, etc. COVID-19 modeling plays an irreplaceable role in almost every aspect of our fight of the COVID-19 pandemic, in particular, in characterizing the intricate nature of COVID-19 and discovering insights for the virus containment, disease treatment, drug and vaccine development, and mitigating its broad socioeconomic impact.

In fact, according to the WHO-collected global literature on coronavirus disease COVID-191, 2020 has seen about 160k references (collected on 22 Feb 2021) published on COVID-19-related medical/biological issues, computer science, economics, environment, policy, engineering, etc. to understand and study SARS-CoV-2 and COVID-19 and their relevant problems. The computer science communities alone have contributed about 4k publications including modeling COVID-19 by classic and deep analytical and learning methods. While several surveys on modeling are available, they focus on reviewing progress from specific perspectives, e.g., on general AI and machine learning applications for specific aspects [Nazrul Islam et al., 2020; Nguyen, 2020] such as forecasting [Rahimi et al., 2021], virus detection, spread prevention, and medical assistance [Shahid et al., 2020], epidemic prediction, clinical diagnosis, policy effectiveness and contact tracing [Mao et al., 2020] and disease detection and diagnosis, virology and pathogenesis, drug and vaccine development, and epidemic and transmission prediction [Chen et al., 2020a] and by specific methods such as computational intelligence [Tseng et al., 2020], computer vision [Ulhaq et al., 2020], and statistical models [Mohamadou et al., 2020]. These reviews pave a picture of what happened in their selected scope on few references. We have not find a comprehensive and critical analysis of the intricate challenges of the virus and disease, data and modeling, and no work has been informed by the above WHO COVID-19 literature.

Going beyond a specific scope and a small number of references usually covered in a survey, this paper builds on the statistics and insights from analyzing their titles and abstracts of the WHO-listed 160k full references, some 12k references particularly on modeling, and about 32k with full text. Based on both a deep keyword-based similarity analysis of the above references and intensive literature review, we categorize the characteristics and challenges of COVID-19 disease, data and modeling in Section 2. A transdisciplinary landscape is

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1https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/
formed to categorize and match both COVID-19 modeling tasks and objectives and their corresponding modeling methods, which are summarized in Sections 4 and 3, respectively. Section 5 further discusses significant gaps and opportunities in modeling COVID-19.

2 COVID-19 Disease, Data and Modeling Complexities

Here, we summarize the main characteristics and challenges of the COVID-19 disease, data and modeling.

2.1 Disease Characteristics

Modeling COVID-19 is highly challenging owing to its poorly-understood to unknown virus and disease with unique clinical and epidemiological characteristics [Holmdahl and Buckee, 2020]. Despite common epidemic clinical symptoms like fever and cough [Guan et al., 2020], COVID-19 presents many other sophisticated characteristics that make it more contagious but challenging for containment. (1) High contagiousness and rapid spread: Showing higher reproduction number $R_0$ (larger than 3.0) at the initial stage than SARS (at 1.7-1.9) and MERS (< 1) [Petrosillo et al., 2020], e.g., a median reproduction number 5.7 at a 95% confidence interval (CI) [3.8, 8.9] for the early breakout in Wuhan [Sanche et al., 2020]; 3.60 (95% CI: 3.49 to 3.84) in Italy by an SEIR (susceptible-exposed-infected-recovered)-like transmission model [Gatto et al., 2020]; and 3.1 (95% CI: 2.4 to 5.5) [de Souza et al., 2020] in Brazil; SARS-CoV-2 is more transmissible than SARS-CoV (severe acute respiratory syndrome coronavirus) and MERS-CoV (Middle East respiratory syndrome coronavirus) although it shares 79% genome sequence identity with SARS-CoV and 50% with MERS-CoV respectively [Lu et al., 2020; Esakandari et al., 2020]. (2) A wide range of incubation period: An average pre-symptomatic length of 5-6 days but lasting up to even 14 days [Organization, 2020; Yu et al., 2020; Lauer et al., 2020] in comparison with SARS (4.4 days) and MERS (5.5 days) [Park et al., 2020], requesting long quarantine time. (3) A large quantity of asymptomatic infections: Despite remaining uncertain, there could be about 30% of entire population [Ravindra et al., 2020] and 20% of infections [Buitrago-Garcia et al., 2020] who are asymptomatic, making large amounts of undocumented infections and higher infections through asymptomatic and mild-symptomatic individuals [Kronbichler et al., 2020]. (4) High mutation with high contamination: The SARS-CoV-2 variants such as B.1.1.7 and B.1.351 variants emerge with a higher transmissibility [Priesemann et al., 2021] and reproduction rate (increasing 1-1.4 by B.1.1.7) [Volz et al., 2021], challenging existing vaccines, containment and mitigation methods.

While the above summarizes some recent quantification of the COVID-19 disease complexities, it is also noted that the knowledge about the nature of COVID-19 and its virus and their developments is still rather limited. Without knowing its origins, there is much misinformation about the virus and disease and their contagion and interventions [Roozenbeek et al., 2020]. There is weak to no ground-truth about the reality of its infections, symptoms in medical imaging, and mitigation and treatment measures. There are not results reported from joint pathological, epidemiological, biomedical and socioeconomic studies on deeply and systemically understanding COVID-19 virus and disease complexities, common knowledge, and ground-truth.

2.2 Data Sources and Challenges

COVID-19 involves multisource, small, sparse and highly inconsistent-quality data [Latif et al., 2020]. Typical data sources and factors include (1) epidemiological factors (e.g., origin, incubation period, transmission rate, mortality, morbidity, and highly to least vulnerable population, etc.); (2) daily new-infected-recovered-death case numbers and reporting time; (3) quarantine and mitigation measures and policies (e.g., social distancing, and border control) on communities and individuals; (4) clinical, pathological and genomic data (e.g., symptoms, medical facilities, hospitalization records, medical history, medical imaging, pharmaceutical treatments, gene and protein sequences); (5) demographics (e.g., age, gender, racial, cultural background, and habit); (6) social activities and mobility; (7) domain knowledge and precaution guidance from authorities; (8) seasonal and environmental factors (e.g., season, geographical location, temperature, humidity, and wind speed); (9) news, reports and social media discussions; and (10) fake news, rumor and misinformation. Such COVID-19 data are heterogeneous coded in character, text, number and image; in unordered, temporal/sequential and spatial modes; in static and dynamic forms; and with strong characteristics below.

While COVID-19 is pandemic across all regions, its publicly available data are not large, consistent, complete and detailed, showing the following typical characteristics that challenge the COVID-19 modeling. (1) Gaps between reality and documentation: Owing to many reasons related to e.g. pre-symptomatic and asymptomatic infections, testing capability, manual recording, confirmation standard, an evolving understanding and attention of the disease nature, and subjective factors, the reported new-infected-recovered-death cases may be highly divided from their reality and from country to country, their reality may be even unknown. Such gaps may be more apparent in the first wave, the early stage of breakouts, and some countries and regions [Maier and Brockmann, 2020], leading to a likely unknown reality of the pandemic. (2) Acyclic and short range with small size: Except rare scenarios like in the US, most countries and regions report a short-range (2-3 months or even shorter), low-granularity (typically daily), and small-size record of their COVID-19 data. Such data is typically acyclic but not cyclic like having seasonal or periodical patterns as in influenza [Coletti et al., 2018] and recurrent dengue epidemics in tropical countries [Ulrich et al., 2020]. (3) Incompleteness, inconsistencies, inequality and incomparability: Typically, it is hard to find all-round information about a COVID-19 patient’s infection source, demographics, behaviors, social activities (including mobility and in social media), clinical history, diagnoses and treatments, and resurgence if any. COVID-19 public data also present strong inconsistencies and inequality across reporting hotspots, countries and regions, updating frequency and timeliness, case confirmation standards,
collection methods, and stages [Roda et al., 2020]. Data from different countries and areas may be unequal and incomparable due to their distinct coverage, affected by people’s different racism, living habits, applied mitigation policies, and health and medical conditions and protocols. (4) Other issues: Comparing public data from different sources also shows issues like potential noise and manipulations in case numbers, missing values (e.g., unreported on weekends and in the early stage of breakouts), different categorization of cases and stages (e.g., some with susceptible and asymptomatic case numbers), misinformation, and lack of information and knowledge about resurgence and mutation and their difference from the origins.

In conclusion, while increasing amounts of data are available, the publicly available COVID-19 data are in fact poor in terms of quality, quantity, capability and capacity to discover deep insight about COVID-19 nature and impact. It is fundamental and urgent to acquire substantially larger and better quality multisource COVID-19 data so that meaningful modeling can be robustly conducted to disclose intrinsic knowledge and insight about the disease and for better pandemic control.

2.3 Modeling Complexities

The COVID-19 pandemic forms an open complex system with significant system complexities [Wang et al., 2021] including the hidden nature and strong uncertainty, self-organization, dynamics and evolution of the virus, disease and their developments and transmissions, sophisticated interactions and relations to environments and context, differentiated infection on individuals and communities, and significant emergence of consequences and impacts on society and almost every part of the world. However, the publicly available poor and small COVID-19 data do not explicitly display a complete picture and sufficient indication of the above complexities and its intrinsic epidemiological attributes, transmission process, and cause-effect relations. It is thus challenging to undertake sound, robust, benchmarkable and generally-useful modeling on such potential-limited data. Below, we summarize several major complexities in modeling COVID-19.

(1) Ambitious modeling objectives on low-quality small COVID-19 data: As shown in Section 3.2, many business problems and objectives may be addressed by modeling COVID-19. However, the strong constraints in COVID-19 public data shown in Section 2.2 significantly limits such potential. Models have to carefully define learnable objectives, i.e., what can be learned from the data, acquire the essential and feasible data, or leverage the data poverty by more powerful modeling approaches. For example, when a model is trained on one country’s case numbers, its application to others may produce unfair results owing to their data inequality. Another example is how to combine multisource but weakly-connected data for meaningful analysis and results. (2) Disclosing factual relations between weakly-coupled COVID-19 factors: COVID-19 is affiliated with many personal, social, health/medical, political and other factors, dispersedly reflected in multisource data and systems. It may be reasonable to say that these multi-factors are coupled strongly or weakly, locally or globally, explicitly or implicitly, subjectively or objectively, statically or dynamically, and essentially or accidentally in the virus and disease formation, development, influence, and evolution. COVID-19 modeling needs to disclose such sophisticated factor couplings, though they are not obvious in multisource observations. (3) Complex modeling with weak domain knowledge and ground-truth: The weak to no-firm knowledge and ground-truth about COVID-19 and its medical confirmations and annotations and the poor-quality data make modeling frustrated. This limits the capacity and richness of hypotheses to be tested on the data. It is not surprising that rather simple and classic analytical and learning models are predominantly applied by medical and biological scientists to verify specific hypotheses, e.g., various SIR models, time-series regression, and traditional machine learning methods [Giordano et al., 2020; Chen et al., 2020b; Shahid et al., 2020] occupy the top-80 keywords-based methods in the 160k WHO-collected references. In contrast, statisticians and computer scientists tend to enforce overparameterized models, over-complicated the hypotheses, or over-manipulate the data, resulting in highly specific results and over- or under-fitting issues. (4) Powerful models on potential-limited available data: Due to the above observations, COVID-19 modelers have to carefully design and apply powerful models such as overparameterized deep neural networks, SIR variants and hierarchical Bayesian networks on the highly limited and poorly-coupled small COVID-19 data. They have to avoid under/over-fitting, demonstrating modeling complexity rather focusing on disclosing underlying nature and insight. It is rather too early to discover actionable knowledge and intelligence from the COVID-19 data and modeling [Booth et al., 2020; Tovstiga and Tovstiga, 2020].

3 COVID-19 Modeling Landscape

Despite only tackling the COVID-19 challenges for about one year, the global scientific communities have been very productive in studying COVID-19, its virus and their interventions and impacts. This section summarizes the statistics, roadmap, and problem-solving objectives of COVID-19 modeling.

3.1 A Roadmap of COVID-19 Modeling

Some statistics of the WHO COVID-19 literature. Our keyword-based similarity analysis using the SciBERT pre-trained vector [Beltagy et al., 2019] and domain-expert filtering of the 160k literature with some 12k on modeling comes up with the following brief statistics of extracted keywords about the COVID-19 business concerns, disciplinary and modeling-specific keyword distributions, as shown in Figures 1 and 2. (1) Contributing disciplines: As shown in the blue curve in Figure 2, some 127k references on medical and biological science (BM), 4k on computer science (CS), 3k on economics (Eco), 900 on environment (Env) and policy (Pol) respectively, with remaining 23k by other disciplines (Oth); the red curve further shows, among the 12k modeling references, some 9k references are from BM, 1.8k from CS, 450 from Eco, and 1.4k from others. (2) Highly-concerned
business problems: Figure 1 shows the word clouds of all 160k (in figure (a)) and 12k (in figure (b)) modeling-specific WHO-listed COVID-19 literature. Epidemic outbreak, infection, transmission, intervention, diagnosis, treatment, mortality, and response strategies form top business concerns. (3) Highly-ranked modeling methods: As the word cloud shown in Figure 1(b) and the modeling-specific literature distribution shown in the green curve in Figure 2, time series (TS) models (about 4.5k references on various regression and forecasting methods), classic machine learning (ML) methods (3.5k on methods e.g. ANN, statistical models, tree models, SVM, transfer learning, NLP methods, and reinforcement learning), epidemiological models (EM, about 1.9k on SIR and their variants and other methods), deep learning methods (DL, 1.1k on methods e.g. CNN, DNN, LSTM/RNN and GAN-based networks), and simulation (Sim, about 250) are the top five. (4) Active research countries and regions: US, China, Italy, UK and India are among the top-5 contributing countries to the 32k full-text-available references with country information, where Europe, Asia, America, Africa and Oceania contribute to 36.5%, 34%, 24%, 3% and 2.5% of the total publications, respectively.

The research landscape of COVID-19 modeling. Transdisciplinary modeling methods have been explored to address broad-based COVID-19 issues. Figure 3 summarizes a transdisciplinary research landscape with mostly applied methods to address the major business concerns and objectives shown in the references. The categorization of COVID-19 modeling. The flood of COVID-19 modeling presents strong features: multi-
disciplinary; epidemiologically domain-dominant; model-driven with applications of various families of models and methods; case study-based by testing specific hypotheses or illustrating results from specific settings, scenarios or data; data-driven focusing on analyzing specific COVID-19 data and findings on the data. Below, we categorize COVID-19 modeling in terms of business objectives and tasks in Section 3.2 and modeling methods in Section 4.

3.2 Objectives of COVID-19 Modeling

We here summarize the main business problems and objectives targeted in the COVID-19 modeling. Figure 1(a) gives us a clear indication of the top business terms concerned in the 160k total and 12k modeling-focused references collected by the WHO. The top-ranked keywords include the COVID-19 and coronavirus pandemic outbreak, spread, infection, transmission, factors, symptom, characteristics, treatment, diagnosis, mortality, their risk and effects, as well as their analysis and research. Below, we categorize the main concerns and objectives, Table 1 further summarizes them with their associated data factors and representative modeling methods.

Characterizing and predicting the COVID-19 epidemic and transmission. An imperative challenge is to understand the COVID-19 epidemic mechanisms and transmission process, infer its epidemiological attributes, and reveal how the virus spreads spatially and socially [Adiga et al., 2020]. The majority of COVID-19 modeling focuses on exploring the source and spectrum of COVID-19 infection, clinical and epidemiological characteristics, tracking its transmission route, and forecasting case development trend and the peak number of infected cases and disease transmission [Chan et al., 2020; Wu et al., 2020a; Wu et al., 2020b]. The findings are expected for disease precaution, virus containment, mitigation effect analysis, and medical resource planning, etc.

Diagnosis, case identification and contact tracing. Given the strong transmission and reproduction rates, high contagion, and sophisticated but unclear transmission routes of COVID-19 and its virus, it is crucial to immediately identify and confirm exposed cases and trace their origins and contacts so as to proactively implement quarantine measures and contain their potential spread and breakout [Ng et al., 2020]. This is particularly important during the varying incubation periods (2 - 14 days) which are asymptomatic to mildly symptomatic yet highly contagious. In addition to chemical and clinical approaches, the COVID-19 identification by analyzing biomedical images, genome and symptoms, and social activities, mobility and media communications turns out to be also essential [Udagama et al., 2020].

Modeling the efficacy of pharmaceutical and non-pharmaceutical interventions. On one hand, pharmaceutical measures, drug and vaccine developments play fundamental roles [Zheng et al., 2020c]. On the other, to control the outbreak of COVID-19, governments adopt various non-pharmaceutical interventions (NPIs) e.g. travel ban, border control, business and school shutdown, public and private gathering restrictions, mask-wearing, and social distancing. Limited research has been conducted on verifying the effects of these measures and their combinations on containing the virus spread and case number development [Tian et al., 2020; Dehning et al., 2020; Brauner et al., 2020], while rare outcomes are available on the threshold and effects of COVID-19 vaccinations and herd immunity. More robust results are expected to inform medical and public health policy-making on medication, business and society.

Understanding pathology for drug development. By involving the domain knowledge of virology, pathogenesis, genomics and proteomics and collecting pathological testing results, gene sequences, protein sequences, physical and chemical properties of SARS-CoV-2, drug information and its effect, modeling has been conducted to correlate drugs with protein structures for COVID-19 drug selection and development by CNN, LSTM, MLP and DNN-based drug-target interactive networks and knowledge maps [Beck et al., 2020], predict protein structures by DNN [Senior et al., 2020], identify viral genomes and classify new pathogens by sequence analysis and classifiers [Randhawa et al., 2020], detect respiratory viruses and design nucleic acid detection [Metsky et al., 2020], screen candidate biological products by multitask DNN [Hu et al., 2020a], and generate new molecular structures by deep models [Zhavoronkov et al., 2020] for immunity responses, drug development and mutation intervention.

Modeling the resurgence and mutation. Our current understanding of COVID-19 resurgence and mutation is very limited while the British and South African mutations show higher contagion and complexities [Grubaugh et al., 2020; Grubaugh et al., 2021]. COVID-19 may indeed become another epidemic disease staying with humans for a long time. Imperative research is expected on quantifying the resurgence conditions, controlling potential resurgence after lifting certain restrictions and reactivating businesses and activities [López and Rodó, 2020; Pedro et al., 2020], distinguishing characteristics and containment measures from waves [Fan et al., 2020; Grech and Cuschieri, 2020; Aleta and Moreno, 2020], and preparing for and predicting resurgence, mutation and their countermeasures [Aravindakshan et al., 2020].

Impact modeling. While the COVID-19 pandemic has changed the world and made significant overwhelming influence on almost all aspects of our life, society and economy,
quantifying their impacts has rarely been studied. COVID-19 negative impact modeling may include (1) economic impacts on growth and restructuring [Bank, 2020], (2) social impact on people’s stress, psychology, emotion, behavior and mobility [Pedrosa et al., 2020; Xiong et al., 2020], and (3) transforming business processes and organization, manufacturing, transport, logistics, and globalization [Vo and Tran, 2021; Seetharaman, 2020]. In contrast, it would also be interesting to model its ‘positive’ influence on (1) enhancing the wellbeing and resilience of individuals, families, society and work-life balance [Prime et al., 2020], (2) digitizing and transforming work, study, entertaining and shopping [Soto-Acosta, 2020], (3) restructuring supply-demand relations and supply chains for better immediate availability and demand-satisfying [del Rio-Chanona et al., 2020], (4) promoting research and innovation on intervening in global black-swan disasters like COVID-19 and its impacts [Zhang et al., 2020], and (5) enhancing trust and development in science, medicine, vaccination and hygiene [Plohl and Musil, 2021].

Other impact modeling tasks include analyzing the relations between COVID-19 containment and income level particularly concerning lower-income and disadvantaged groups, healthcare capacity and quality, government crisis management capabilities, citizen-government-cooperation, and public health and hygiene habits.

4 COVID-19 Modeling Methods

As shown by the word cloud in Figure 1(b) of the 12K WHO-collected modeling references, epidemiological modeling, artificial intelligence and data science play predominant roles in the COVID-19 understanding, analysis, modeling and prediction. By categorizing the top-ranked modeling methods, we find that mathematical methods including time series analysis, general machine learning methods, epidemiological modeling, deep learning, and simulation form the mostly-used approaches to addressing the aforementioned objectives and to simulate, characterize, regress and forecast COVID-19. Below, we briefly summarize the application of these relevant modeling methods in COVID-19 modeling. Table 2 further compares major methods and their pros and cons in modeling COVID-19.

4.1 COVID-19 Time Series Analysis

Time-series analysis contributes most (about 3k of the 160k references) to COVID-19 modeling. As shown in Figure 1(b), regression model, linear regression, logistic regression are mostly eye-catching. Many linear and nonlinear, univariate, bivariate and multivariate analysis methods have been intensively applied to the regression, trend and forecasting of new, susceptible, infectious, recovered and death case numbers. Popular methods include linear regression models such as ARIMA [Tandon et al., 2020], logistic regression [Wang et al., 2020b], COX regression [Schwab et al., 2021], multi-
| Objective                  | Modeling factors                                                                 | Approach                                                                 | References                                                                 |
|----------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Epidemic transmission      | Epidemiological factors (e.g., origins, incubation period, transmission rate,     | Regression, compartmental models, time/age-dependent compartmental models,   | [Giordano et al., 2020; Weitz et al., 2020; Aguiar et al., 2020; Chen et al., 2020; Singh and Adhikari, 2020; Zhou and Ji, 2020; Crokidakis and others, 2020; Biswas and Sen, 2020; Peng et al., 2020] |
|                            | mortality, morbidity, and highly to least vulnerable population, etc.), daily    | probabilistic compartmental models, etc.                                  |                                                                           |
|                            | newly-infected/recovered-death case numbers and reporting time, side information |                                                                         |                                                                           |
|                            | about population, etc.                                                            |                                                                         |                                                                           |
| Interventions              | Intervention measures, quarantine and mitigation measures and policies on         | Regression, customized compartmental models, Bayesian hierarchical models   | [Brauner et al., 2020; Prem et al., 2020; Aguiar et al., 2020; Giordano et al., 2020; Tian et al., 2020; Maier and Brockmann, 2020; Flaxman et al., 2020; Dehning et al., 2020; Lai et al., 2020] |
|                            | communities and individuals, epidemiological factors, daily new-infected/recovered- | models, stochastic compartmental models, etc.                            |                                                                           |
|                            | death case numbers and reporting time, social activities, communications          |                                                                         |                                                                           |
| Diagnosis                  | Clinical, pathological and genomic data (symptoms, medical facilities,           | Regression, statistical learning, decision trees, random forest, various   | [Wang et al., 2020a; Chikina and Pegden, 2020; Basu et al., 2020; Cohen et al., 2020; Minae et al., 2020; Das et al., 2020; Khalifa et al., 2020; Apostolopoulos and Mpesiana, 2020; Mukherjee et al., 2021] |
|                            | hospitalization records, medical history, medical imaging, physical and chemical  | deep neural networks (e.g., CNN, DNN, GAN, DenseNet), etc.                |                                                                           |
|                            | measures, pharmaceutical treatments, gene sequences, proteins), mobility and     |                                                                         |                                                                           |
|                            | contacts, etc.                                                                   |                                                                         |                                                                           |
| Resurgence and mutation    | Daily new-infected/recovered-death case numbers and reporting time, quarantine   | Compartimental models, simulation models, compartmental models with        | [Leung et al., 2020; Aravindakshan et al., 2020; Cacciapaglia et al., 2020; López and Rodó, 2020; Pedro et al., 2020] |
|                            | and mitigation measures and policies on communities and individuals, social      | regression, epidemic Renormalisation Group, etc.                          |                                                                           |
|                            | activities and mobility, seasonal and environmental factors (e.g., season,      |                                                                         |                                                                           |
|                            | geographical location, temperature, humidity, and wind speed)                    |                                                                         |                                                                           |
| Influence and impact       | Quarantine and mitigation measures and policies on communities and individuals,  | Statistical analysis, questionnaire methods, age-structured SIR/SEIR     | [Chakraborty and Maty, 2020; Kreps and Kriner, 2020; Li et al., 2020; Sharma et al., 2020; Walker et al., 2020] |
|                            | domain knowledge and precaution guidance from authorities, social activities and  | models, deep neural networks (e.g., BERT and LSTM), simulation models, etc.|                                                                           |
|                            | mobility, demographics (e.g., age, gender, racist, cultural background, habit),  |                                                                         |                                                                           |
|                            | related news, reports, social media discussions, and misinformation.             |                                                                         |                                                                           |

4.2 COVID-19 Machine Learning

Statistical and other general (shallow) machine learning methods form the second popular set (about 2.4k of 160k) for modeling COVID-19 uncertainty, complexities, classification, variation, and prediction. General machine learning methods including artificial neural networks, tree models such as decision trees and random forest, support vector machines (SVM), transfer learning, NLP and text mining methods, genetic algorithms, fuzzy set and reinforcement learning are mostly used in modeling COVID-19 by biomedical, computing and social scientists [Shahid et al., 2020; Mohamadou et al., 2020]. These tools are easy to understand and implement, more applicable than other sophisticated methods (e.g., deep models and complex compartmental models) for the small COVID-19 data.

In addition, statistical learning in particular Bayesian models play critical roles, which take generative stochastic processes to model epidemic contagion in classic epidemic modeling [Andersson and Britton, 2012; O’Neill and Roberts, 1999]. In contrast to compartmental models, statistical models involve prior knowledge about an epidemic disease and their results have confidence levels corresponding to distinct assumptions (i.e., possible mitigation strategies), better interpreting and more flexibly modeling COVID-19 complexities. In COVID-19, for example, hierarchical Bayesian distributions with hidden states and parameters are used to model the causal relationships in their transmission [Niehus et al., 2020; Flaxman et al., 2020]; probabilistic compartmental models [Zhou and Ji, 2020]; Osthus et al., 2019; Hébert-Dufresne et al., 2020] integrate the transmission mechanisms of epidemics with the statistics of observed case data.

4.3 COVID-19 Epidemiological Modeling

Epidemiological models dominate the COVID-19 modeling by epidemic researchers, they are also adopted by computing scientists for expansion or hybridization with other machine learning methods. Such mathematical models incorporate epidemic knowledge and compartment hypotheses into imitating the multi-state transition like between susceptible (S), infectious (I), recovered (R) and death. People in the COVID-19 epidemic may take one of these states at a time-point and may transit from S to I and R if infected at certain
transmission and recovery rates.

The classic SIR model [Kermack and McKendrick, 1927] and susceptible-exposed-infectious-recovered (SEIR) model [Aron and Schwartz, 1984] for other epidemics like measles and Ebola have been adapted, e.g., by adding tailored compartments like quarantine, protected, asymptomatic and immune, to model COVID-19-specific characteristics and mitigation measures [Giordano et al., 2020; Weitz et al., 2020; Aguiar et al., 2020; Crokidakis and others, 2020; Maier and Brockmann, 2020]. Further, time-dependent compartmental models [Chen et al., 2020b; Biswas and Sen, 2020; Peng et al., 2020] capture the evolving COVID-19 epidemiological attributes, i.e., time-variant infection, mortality and recovery rates. Other work also involves side information (e.g., NPIs, age stratification and heterogeneity, and population mobility) in compartmental models [Chikina and Pegden, 2020; Singh and Adhikari, 2020] for their influence on state transition.

### 4.4 COVID-19 Deep Learning

As the flag-bearer technique in the modern machine learning family, deep learning has also been intensively applied to the COVID-19 modeling. Typically, typical applications of deep neural networks include: (1) characterizing symptoms of coronavirus infections by pretrained neural networks; (2) analyzing epidemic dynamics e.g. of breakout tracking [Hu et al., 2020b], effect of quarantine policies on breakout by deep neural networks [Dandekar and Barbastathis, 2020] and global transmission dynamics by a modified autoencoder [Hu et al., 2020c], predicting epidemic size and lasting time, and combining medical information with local weather data to predict the risk level of a country by a shallow LSTM model [Pal et al., 2020]; (3) processing COVID-19 imaging data for diagnosis, quarantine and treatments, e.g. by analyzing chest X-ray images by CNN to screen patients [Das et al., 2020; Mukherjee et al., 2021; Basu et al., 2020], X-ray images by deep transfer learning models [Cohen et al., 2020; Minaee et al., 2020; Khalifa et al., 2020; Apostolopoulos and Mpesiana, 2020], and CT images to identify infected patients [Zheng et al., 2020a]; (4) identifying existing and commercial drugs for drug repositioning [Beck et al., 2020] and vaccine manufacturing [Eisenstein, 2018]; (5) NLP and text mining for emotion analysis in social media and misinformation identification [Li et al., 2020; Sharma et al., 2020; Duong et al., 2020], enhancing epidemic modeling by social media data [Kim et al., 2019], and analyzing the COVID-19 research progress and topic evolution [Zhang et al., 2020]; and (6) other tasks such as virus structure analysis and recording cough/sound signals by smart phones with knowledge from medical experts AI4COVID-19 [Imran et al., 2020].

### 4.5 COVID-19 Simulation

Despite being a small focus, simulation is an essential means to understand, imitate, replicate and test the working mechanisms, epidemic transmission processes, interactions and self-organization between factors, the effect of mitigation measures, healthcare resource allocation, and the evolution and mutation of COVID-19 and its virus SARS-CoV-2. Typical tools include dynamic systems, discrete event simulation, agent-based modelling and reinforcement learning, and hy-
brid simulation [Currie et al., 2020]. For example, a simulation model evaluates the propagation and control of COVID-19 in Australia [Chang et al., 2020], and an AI-driven multisource data system assesses the community risk of COVID-19 [Ye et al., 2020].

4.6 Hybrid and Other Methods
COVID-19 hybrid modeling commonly applies to both multisource COVID-19 data and multi-methods from various disciplines. Examples are compartmental models with their parameters derived/updated by external information like news, mobility, control policies; NLP analyzing and extracting related news as input to LSTM networks to update the infection rate in an epidemic model [Zheng et al., 2020b]; and coupling LSTM with an epidemic model to forecast COVID-19 spread on case data, population density and mobility [Soures et al., 2020].

In addition to the aforementioned methods, other methods and tasks e.g. for innovative pandemic responses are available in the literature. Examples are automated primary care tools to alleviate the shortage of healthcare workers [Tavakoli et al., 2020], expert systems and chatbots for symptom detection and lessening mental health burden [Miner et al., 2020], IoT and smart connecting tools for preventing breakouts, remotely monitoring patients, and prompting enforcement of guidelines and administrative orders to contain future outbreaks [Gupta et al., 2021].

5 Discussion and Opportunities
Though massive efforts have been made in modeling COVID-19, existing work is still in its early stage, focusing on (1) an average description of the population-wise coronavirus and disease’s epidemiological characteristics and the observations from applied mitigation and control measures without fine-grained/microlevel analysis and findings; (2) a direct application of existing (even very simple and classic) modeling methods without COVID-19-specific and optimal modeling mechanisms; (3) data-driven modeling purely motivated by applying advanced models (typically deep models) on COVID-19 data. As a result, it is common that models and modeling results (1) are too specific to be expanded to other countries and scenarios; (2) over- or under-fit to given data and hypothesis settings typically by applying deep models and complex statistical and compartment models on low-quality small COVID data; and (3) a lack of ability and capacity of disclosing intrinsic nature and general insights of the virus, disease and their interventions.

Very limited research has been on (1) trans-disciplinarily integrating best knowledge from biomedical science, pathology, epidemiology, statistics and computing science to address multifaceted challenges in virus, disease, data and modeling; (2) defining modeling objectives and tasks to directly address COVID-19-specific epidemiological, clinical, social, economic or political concerns and their challenges; and (3) developing COVID-19 disease and data challenges-driven modeling methods, benchmarks and evaluation measures.

There are also several areas rarely or poorly addressed in COVID-19 modeling: (1) characterizing the variants of SARS-CoV-2 virus and their effective interventions and impact; (2) modeling the effects of COVID-19 vaccines, pharmaceutical and NPI interventions on infection control, mobility, mental health, society and economy, e.g., the efficacy of vaccinated population percentage on herd immunity, and the effect of variable close-contact interactions and individual actions on epidemic de-escalating; (3) balancing the NPI strength and socioeconomic influence, e.g., the effect of full vs partial business close-down and border control on virus confinement at different stages and for different sectors, and the effect of increasing daily commuting/workforce movement on virus confinement; (4) capturing the temporally evolving interplay and interactions between virus propagation and interventions; and (5) modeling target problems by systemically coupling relevant multisource data and multi-methods, e.g., pathogen-related, societal, environmental and racist factors and disparities between developing and developed countries, age groups, and racists.

Other modeling opportunities include hybridizing (1) coarse-grained and fine-grained modeling, e.g., epidemic modeling by SIR variants to inform further specific NPI’s effect analysis; (2) static and dynamic modeling, e.g., from population-based static epidemic modeling to specific NPI-97 varying and time-varying case forecasting; (3) observable and hidden factors and relations, e.g., multisource-based attributed modeling with deep abstraction and representation of interactions between the multisource factors; (4) local/micro-level and global/macro-level factors, e.g., involving patient clinical and demographic records with their environmental and socioeconomic context in survival and mortality prediction and medical resource planning; (5) domain, data and models for domain-specific, interpretable and evidence-based and actionable findings. These typically involve compound modeling objectives, multisource data, and multi-method ensembles.

6 Conclusion
The COVID-19 pandemic’s short-to-long-term influence and impact on public health (both physical and mental health), human daily life, society, economy and global politics are unprecedented, lasting yet quantified and verified. This review shows the significant gaps and imperative importance of deeply and systematically characterizing COVID-19-related problems and complexities and developing effective, interpretable and actionable models to characterize, measure, imitate; evaluate and predict broad-based challenges and problems and to proactively and effectively intervene in them. Such COVID-19 modeling research proposes many significant challenges to the multidisciplinary modeling communities in the next decade, not only for immediately gaining the intrinsic knowledge and proactive insight about the evolving coronavirus and its disease outbreak, infection, influence and intervention, but also for preparing for tackling future global health, financial, economic, security-related and other black-swan events and disasters.
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