Integrating agent-based disease, mobility and wastewater models for the study of the spread of communicable diseases

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Abstract

Wastewater-based epidemiology was utilized during the COVID-19 outbreak to monitor the circulation of SARS-CoV-2, the virus causing this disease. However, this approach is limited by the need for additional methods to accurately translate virus concentrations in wastewater to disease-positive human counts. Combined modelling of COVID-19 disease cases and the concentration of its causative virus, SARS-CoV-2, in wastewater will necessarily deepen our understanding. However, this requires addressing the technical differences between disease, population mobility and wastewater models. To that end, we developed an integrated Agent-Based Model (ABM) that facilitates analysis in space and time at various temporal resolutions, including disease spread, population mobility and wastewater production, while also being sufficiently generic for different types of infectious diseases or pathogens. The integrated model replicates the epidemic curve for COVID-19 and can estimate the daily infections at the household level, enabling the monitoring of the spatial patterns of infection intensity. Additionally, the model allows monitoring the estimated production of infected wastewater over time and spatially across the sewage and treatment plant. The model addresses differences between resolutions and can potentially support Early Warning Systems (EWS) for future pandemics.

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Introduction

Wastewater-Based Epidemiology (WBE) is an emerging surveillance method with great potential for detecting infectious diseases at an early stage (Zhu *et al.*, 2021). According to the National Academies of Sciences Engineering and Medicine (NASEM), WBE programs are recognized for improving public health protection during pandemics and more investment is expected in this area (NASEM, 2024). Detecting pathogens via wastewater is particularly useful in monitoring disease outbreaks when other disease monitoring techniques are unavailable. It has been used to detect water-borne diseases such as cholera (Tiwari *et al.*, 2024), and COVID-19 (NASEM, 2023). Although continuous wastewater monitoring might be feasible in some countries, intermittent sampling is the only option in most. Infected wastewater samples indicate the presence of the disease and not the number of infected inhabitants in an area, making it difficult to interpret the results and compare multiple locations (Faraway *et al.*, 2022). The complication of estimating the number of infected people from sampled wastewater hinders the design of effective wastewater surveillance in sewage systems and the description of disease outbreaks (Martin *et al.*, 2023; NASEM, 2023). WBE models have the potential to simulate outbreaks and infected wastewater (Torabi *et al.*, 2023), relate it to the actual number of infections in an area, visualize infected wastewater dynamics across the sewage, optimize the design of where and when to sample wastewater for early disease detection and indicate mitigation measures to reduce the spread of disease. In parallel, population mobility models add value for modelling wastewater and diseases. Population mobility modifies the variability of wastewater pollutant loads across the sewage and Wastewater Treatment Plant (WWTP) based on localization of wastewater inflow sites (Atinkpahoun *et al.*, 2018; De la Paz-Ruíz *et al.*, 2023b). Additionally, population mobility impacts the spread of an outbreak directly as high motilities relate to higher numbers of positive disease cases (Badr *et al.*, 2020; Cartenì, Di Francesco and Martino, 2020). However, this requires the integration of disease spread, population mobility and wastewater models.

While physicochemical approaches focus on the processes within the sewer (Freni *et al*., 2010; Verdaguer *et al*., 2014; Cook *et al.*, 2018; Petrucci *et al*., 2019), agent-based models (ABMs) are computational simulations of individual, dynamic and adaptive behaviour agents with multiple characteristics that provide interactions between agent and environment (McLane *et al.*, 2011). ABMs enable testing of different scenarios of such interaction considering both agent and environment characteristics with respect to space and time. Wastewater ABMs are a family of models that allow modelling of the viral load using agent-based principles suited for integrating disease dynamics (Augustijn *et al.*, 2016). Since ABMs are bottom-up models focusing on micro-level autonomous interacting agents, they allow modelling of human wastewater production in space and time (Darbandsari *et al.*, 2020; Oliva-Felipe *et al.*, 2021; Truszkowska *et al.*, 2021; Ngo *et al.*, 2022; Assaad *et al.*, 2023). Disease ABMs can reproduce epidemic curve patterns of outbreaks (Barat *et al.*, 2021; Truszkowska *et al.*, 2021). They can also explicitly model human interactions (at various spatial locations) and the resulting disease diffusion. Although population mobility is relevant for interactions that initiate an outbreak, not all models explicitly integrate mobility (Barat *et al.*, 2021; Truszkowska *et al.*, 2021) that can be modelled by allowing agents to move randomly or using empirical commuting data to simulate their movements. In this case, agent commuting is linked to activities such as commuting to school or work. An ABM for single disease may contain many activities linked to multiple commuting locations (Augustijn *et al.*, 2022), where interactions can occur when agents are at the same location.

Integrating a disease ABM with a wastewater ABM and incorporating population mobility is necessary but challenging since differences with regard to temporal resolution introduce significant complexity. Other challenges include designing a system that effectively schedules agent actions over time and validating outputs when data are insufficient (An *et al.*, 2021; Heppenstall *et al.*, 2021). Wastewater models work with high-resolution temporal intervals representing short-term wastewater pollutants variability, something that requires the development of event-based modeling to support the development of wastewater sampling strategies. A discrete-event ABM can make the simulated temporal aspect more accurate and detailed than a tick- or time-step-based ABM approach, a granularity that is particularly useful when designing wastewater sampling schemes. In contrast, disease ABMs are often daily representations divided into time block executions (ticks or time-steps) tracked at a 24-hour temporal resolution (Barat *et al.*, 2021; Truszkowska *et al.*, 2021). Dividing days into blocks representing various activities is common in modelling interactions by ABMs (An *et al.*, 2021; Heppenstall *et al.*, 2021), but this requires a number of time-steps per day (three or four) delivering daily outputs. However, as this resolution does not match the multi-temporal variability of wastewater, the temporal resolution differences between models must be solved to integrate mobility, disease and wastewater ABMs. In response to the abovementioned needs, we developed a model integrating disease; population mobility; and wastewater (integrated disease-population-mobility-wastewater, DMW) data supporting the study of multiple diseases. This was done by integrating a disease ABM with a validated Domestic Wastewater (DW) ABM (De la Paz-Ruíz *et al.*, 2023a). The integrated DMW model was developed with discrete-events to address differences in resolution between the models.

Materials and Methods

Model description and purpose

The DMW model is an ABM simulating both disease diffusion and wastewater production via a set of agents related to inhabitants in an area. Since interactions between people facilitate disease diffusion, a susceptible-infected-recovered ABM model was created and integrated into the DW base model to create the DMW model. The parameters of the disease model are shown in Table 1, which can be adapted based on the characteristics of the disease in question. When infected, inhabitants in the area produce infected

Table 1. Parameters of the disease model (*e.g.*, for a COVID-19 case).

Parameter	Initial value	Description
Duration of simulation	30 days	The ABM runs for one month.
Contact rate	10%	Risk of an inhabitant agent contacting others.
Disease status	Susceptible	Susceptible, infected, or recovered.
SI interactions	4	Maximum range of new possible infections produced by a single infected inhabitant.
Starting spread	2 days	Days after an infected inhabitant starts spreading the disease
Starting sick leave	1 day	Days after infection that an inhabitant interrupts mobility.
Infected stools (range)	2-3 weeks	Weeks that an inhabitant keeps producing infected stools after recovering.
Initial infected cases (N)	5 individuals	Randomly assigned in the population.
Transmission rate (β)	1.25	The average value of the range (0.3-2.2).
Recovery rate (γ)	0.2	The recovery rate is 1/infection duration.
Duration of infection (D)	5 days	Days that an inhabitant may infect others.
Secondary cases (I)	None	Infection cases that are not initial.

ABM, agent-based model; SI, susceptible-infected.

wastewater that travels over the network to a WWTP. The model allows for the comparison between disease outbreaks and produced infected wastewater at various places along the sewer network. The comparison facilitates the interpretation of wastewater samples. The DMW model has three components: i) the disease model; ii) the population mobility model; and iii) the wastewater model. A detailed description of the complete model is provided in the supplementary material.

The validated DW-ABM is the base model used to simulate the spatiotemporal dynamics of population mobility and wastewater production (De la Paz-Ruíz *et al.*, 2023a). The DW-ABM is a suitable model for integrating wastewater and a disease ABM as the model allows for interlinking an outbreak in the population, which is required to produce infected wastewater. In particular, the DW-ABM can track multiple types of wastewater events, such as stool production and its motion in the sewage produced at the individual level, with the potential to reflect not only the disease spread but also population mobility and the changing location of the infected wastewater. This integration facilitates monitoring levels of infected wastewater at multiple locations. The wastewater particles provide information on whether an inhabitant of an area is infected or not, which demonstrates the integration between the disease and wastewater model, as well as providing the production (in a block) of the wastewater in a WWTP, with timestamps and wastewater quality.

Entities

The DMW environment includes houses, schools, workplaces, neighbourhood blocks, sewage networks, maintenance holes and the WWTP. Table 2, modified from (De la Paz-Ruíz *et al.*, 2023a), describes the agent and environment entities in detail. The model contains two types of agents: the inhabitants in the area and the wastewater particles. The National System of Statistical and Geographical Information (INEGI) in Mexico provided the Census data (INEGI, 2020), while a technique to generate disaggregated data (Lovelace & Dumont, 2018; De la Paz-Ruíz *et al.*, 2021) was used to obtain individual inhabitants. The inhabitants are distributed across houses in the area based on the national census data, which includes information on their gender, age, occupation and education. In the model, wastewater particles are also treated as agents, in this case representing pollutants such as Total Suspended Solids (TSS), the main indicator linked to stool events. Wastewater particles hatch from the inhabitants, representing the use of water appliances, such as toilets, kitchen sinks, showers and washing machines.

Variables

The most relevant variables of the inhabitant agents in the DMW model are their health status, infection time and location. Inhabitants' health status can be susceptible, infected or recovered. Their location is home, school or work. The health status is the most relevant variable for wastewater particle agents. Other inhab-

Table 2. Entities of the DMW model.

Unit	Variable	Description	Possible value
Inhabitant	Age	Age category	18-4
	Study	Attend school	Yes
	Health	Health status	Infected
	Infection time	Date and time of infection	21-03-2022,10:30:00
	School level	School level	High school
	Work	Actively working	Yes
	Gender	Inhabitant sex	Female
	CVEGEO	Block location (geographic ID)	1302700010105004
	ID	Individual ID	01750
	Location	Current location	Home, school, work
Domestic wastewater	DW type	Type of water appliance	Stools from toilet
	Disease	Health condition	Infected
	Infection time	Date and time of infection	21-03-2022, 10:30:00
	DW	DW quantity	9 litres (L)
	DW quality	DW pollutants: COD and TSS	453 mg/L
	CVEGEO	Block location	1302700010105004
	ID	Individual ID	01750
	DW speed	Traveling particle speed	1.8 m/s
	Travelling path	Sewage network node	Node 2020
House	House id	House ID	304
	CVEGEO	Block location	1302700010105004
Block	CVEGEO	Block location	1302700010105004
Economic point	ID	Economic point ID	7996840
	CVEGEO	Block location	1302700010105004
	Worker	Average number of workers	3, 5, 15….
	School	School in this point	High school
Sewage network	Node	Connecting nodes	Node 11
	Travel path	Path to move DW particle	Node 684
Treatment plant	Final station	Final destination of the travel-ling path	-

CVEGEO, Geostatistical identifier of neighbourhood blocks; ID, identification; DW, domestic wastewater; COD, Chemical Oxygen Demand; TSS, total suspended solids.

itant agent information is also transmitted to the wastewater particles, such as infection time and the type of wastewater produced (*i.e.* urine or stool). Table 2 in the supplementary material describes all agent and environment variables.

Actions and interactions

The use of water appliances leads to wastewater production. Every workday, inhabitants, depending on their age and work status, will either be at work, in school or staying home. Appliances are used at locations where this agent produces wastewater, leading to particles moving over the sewage network until they reach the WWTP. The inhabitants interact with each other each moment they meet at the various places that they simultaneously occupy, resulting in disease transmission. The sub-models section in the supplementary material describes the details of action and interaction for each sub-model.

Figure 1a highlights the direct link of the essential interactions between the disease, mobility, and wastewater models. Two processes are crucial for this integration: breaking commuting patterns due to illness and the infection of wastewater particles. The start of the infectious period for an inhabitant is defined by the 'starting spread' parameter in the disease sub-model. The 'start sick leave' parameter defines the time when infected inhabitant agents stop commuting. After the 'duration of infection' has passed, the recovered inhabitants resume their daily mobility. When inhabitant agents are infected, they are assumed to transmit the infection to the DW particle agent. The status of a wastewater particle can be susceptible, infected or recovered. Not all appliance usage leads to infected wastewater; for example, although a dishwasher is relevant for modelling wastewater pollutants, its use does not transfer

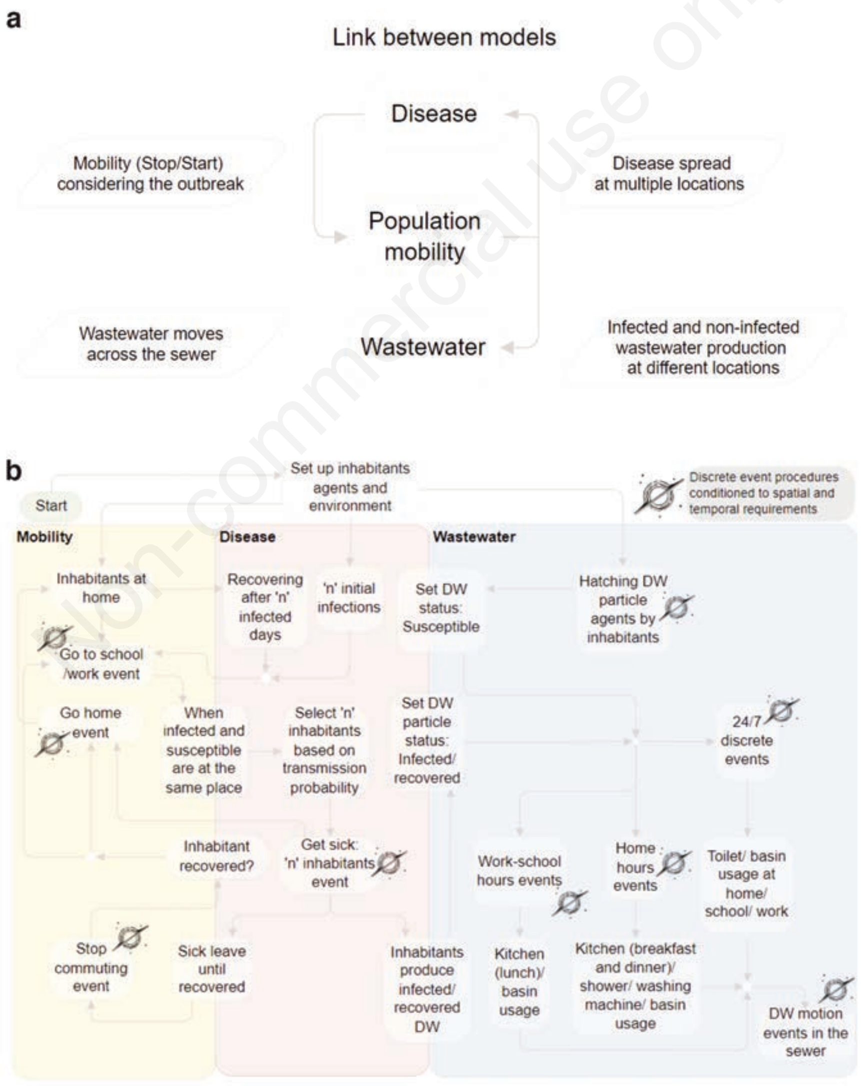

Figure 1. Integration of disease, mobility and wastewater models: **a**) representing a general modular links between the sub-models; **b**) essential procedures linking the DMW discrete event ABM. The agent actions are conditioned to spatial and temporal conditions for executing the individual events.

infection. Only the use of toilet events produces infected wastewater. Recovered inhabitants may still produce infected wastewater particles after recovery, as defined by the 'infected stool range' parameter. Figure 1b shows the details of the essential interactions between the discrete ABM procedure events in the the sub-models. The ABM procedures cover the relationships between mobility, disease and wastewater, with the interactions shown in Figure 1b as procedures on the edges of two sub-models (shown in different colours). For instance, the procedure 'set DW particle status' represents a transition from the disease to the wastewater sub-model by considering the health condition of the inhabitants in the area, which is further transmitted to the DW particle.

The temporal aspect

The scheduling mechanism of the system executes events dynamically based on different probabilities assigned to various event types. The number of events or actions that each inhabitant agent executes varies depending on the dynamics of each model. Events primarily follow realistic probabilistic distributions for wastewater production (De la Paz-Ruíz *et al.*, 2023a), *i.e.* there is an 80% probability that an inhabitant produces stools using the toilet at least once a day. The DMW model concurrently captures the number of infected inhabitant agents and their infected wastewater at the targeted case study as outputs. DMW events are actions the agents execute and can be visualized in a spatiotemporal map series showing neighbourhood blocks, households, maintenance holes and catchment levels.

The DMW model was developed in NetLogo (Wilensky, 1999), a software for ABMs that uses a temporal tick counter for executing procedures. By default, NetLogo does not schedule isolated events (or agent actions) in date-time format (Wilensky, 1999). The DMW model uses the NetLogo time extension (Sheppard *et al.*, 2022) to execute discrete-events for each inhabitant and DW particle action. The time extension allows dynamic scheduling of actions in explicit date-time format, individual temporal actions and continuous tracking when events occur (Sheppard *et al.*, 2020). The temporality with discrete-events can deliver results at multiple temporal intervals, *e.g.*, 6, 12, 30 or 60 minutes. As a result, the DMW model does not have a fixed temporal resolution, such as a daily resolution. Instead, each event is temporally and spatially scheduled and recorded. For instance, the model applies a moderate probability for stool production events throughout the day, particularly scheduled after mealtimes.

Discrete events allow the detection of patterns at multiple spatiotemporal resolutions. For instance, the DMW model enables the study of DW variability at high-resolution temporal events (minutes to hours), which provide crucial information during wastewater surveillance sampling making it possible to avoid collecting non-infected wastewater. In other words, the availablity of high-resolution spatiotemporal heterogeneity in the DMW model enables more sustainable wastewater surveillance sampling by opening the possibility of proposing precise times and places for collecting wastewater. These resolutions are also relevant for detecting unknown patterns of a phenomenon's behaviour that are undetectable when multiple spatiotemporal resolutions are unavailable. Infected wastewater can be aggregated into a daily time-steps, comparing disease cases at multiple locations. All outputs generated were processed using R code scripts (De la Paz-Ruíz *et al.*, 2024) to compare daily disease cases and infected wastewater.

Model outputs

The simulated discrete events (individual agent actions) required post-processing to generate outputs. We defined three post-processing steps, each representing an output generated by multiple runs of the DMW model to guarantee consistent results. Detailed information of the post-processing is provided in the supplementary material in the sub-model section. The following model outputs allowed us to analyse the integration between the models and provide data to analyse the outbreak, population mobility and infected wastewater. We used the DMW model for a COVID-19 to simulate disease spread and infected wastewater output. The parameters for this case study are shown in Tables 1 and 2. The three main outputs of the model (all derived from 25 simulation runs) confirmed successful integration, each targeting a sub-model. Four disease configuration outputs of the COVID-19 outbreak were delivered by varying the transmission probabilities (β) and the susceptible-infected (SI) interactions to verify DMW model's consistency and outbreak's behaviour. With the wastewater model considering the prevalence of infected wastewater, the disease model was tested four times with the transmission rate β (0.05, 0.1, 0.1, and 0.4) and the number of interactions SI (1, 2, 4, 4) changed. We evaluated: i) simulation runs that led to so-called die-outs, i.e. the state when the disease no longer spreads; ii) the number of infected inhabitants in the area and the number of infected wastewater particles coming from infected stools; iii) the duration of the outbreak; and iv) the shape of the epidemic curves.

The outputs verified the model integration with the disease when analysing the variations in population mobility during the disease diffusion. The final output represents the integration of the three sub-models, as the infected wastewater variable can only be produced if the disease and mobility models are integrated into the wastewater model.

Results

COVID-19 outbreak

Figure 2 shows that the outbreak range occurred between approximately 2022-03-22 and 2022-03-31. In most cases, there was a daily infection average of 0.4 to 0.8 per household per run (or 10 to 20 infections per household in 25 runs), with some outliers between 1.6 and 2 (or 40 to 50 infections per household in 25 accumulated runs). It can also be observed that the southern area of the locality had a higher infection density. Figure 2 and the census data show that high infection densities can be largely explained by the significant number of students who were infected during school interactions and then returning home to their respective neighbourhood blocks. The map series also allowed us to appreciate the outbreak's evolution, providing the spatial perspective, which is absent in the normal graph of an epidemic curve.

Figure 3 shows the simulated time graphs of disease cases and wastewater infection levels. The first column shows the presence of the generated infected stools and assumes that the population keeps producing infected stools for some time after recovery, a characteristic of SARS-CoV-2. The second column shows the presence of infected stools without SARS-CoV-2 prevalence after the agents have recovered (when an inhabitant agent recovers from infection, the production of infected stools immediately stops). The last column shows the count of infected inhabitant agents. The simulated outbreak in Figure 3d defines the disease variables that represent a typical COVID-19 outbreak.

Based on Figure 3, agent disease die-outs are represented in the figures as dots on the zero line, meaning that the disease does not spread in every simulation run. More die-outs are expected with lower transmission rates (β) and fewer interactions (SI) with other agents, reducing the likelihood of an infected inhabitant agent transmitting the disease. Die-outs occur in experiments a, b and c but not in experiment d. The total number of accumulated infected inhabitant agents varies across the four experiments (around 170, 270, 280 and 350, respectively). This is reflected in peak values of 0–65 (experiment a), 0–100 (experiment b), 0–90 (experiment c) and 150–250 (experiment d). Similarly, at the peak of the epidemic curves in Figure 3, the values (positive infected events) for experiments a through d were 0–95, 0–150, 0–125 and 190–250, respectively, for infection prevalence and 0–50, 0–85, 0–100, and 100–200, respectively, without infection prevalence.

In all experiments, the initial infections started in March 2022. The simulation ended when no new infections were generated. When considering the duration of the outbreak, the outbreak lasted until 7 May (an estimated 47 days) for experiment a, until 18 April (an estimated 30 days) for experiment b, until 7 May (an estimated 50 days) for experiment c and until 8 April for experiment d (about 20 days after the initial cases were introduced). There was also a clear differences in the shape of the epidemic curve. With increased transmission probabilities (β) and inhabitants that can be infected in an interaction (SI), the curves became shorter and the peaks higher. The difference in curve shape between the infected

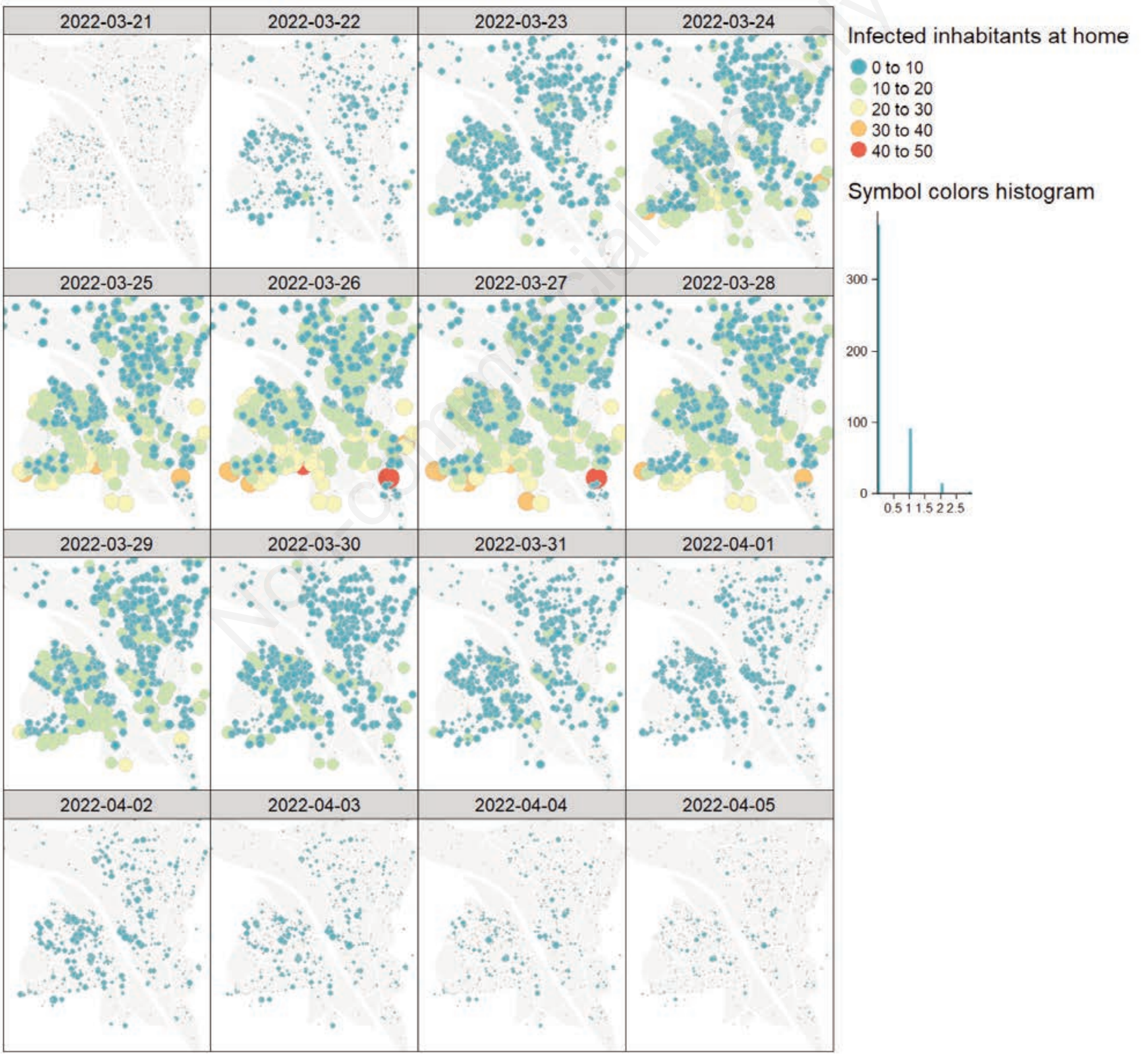

Figure 2. Mapping the density of infected inhabitants at households over time. The figure represents the sum of 25 simulations showing robust results and highlighting the spatial heterogeneity of the households. Disease variables β = 0.4, and S = 4 are used.

stools with and without SARS-CoV-2 prevalence was evident in experiment d. Modelling SARS-CoV-2 prevalence is useful for determining that viral loads in wastewater can be expected to be prolonged even if the population has already recovered. Assuming that recovered inhabitant agents contribute to this value, the peak is flattened, with high values recorded over six days, compared to only three days in the experiment without extended excretion. The rows in Figure 3a, b, c and d represent the different transmission probabilities and the number of infected individuals. Figure 3 a shows that the epidemic curves sank to approximately 75 infected inhabitants at the outbreak peak. In contrast, the duration of the outbreak spaned three months, differing from Figure 3d, which spaned 20 days. A comparison between the rows of Figure 3 also shows that the disease parameter β had a greater influence than the SI parameter in altering the pattern of the epidemic curve. For instance, a comparison of 3 c and 3 d, with β values of 0.1 and 0.4, respectively, shows that the outbreak peak sank from 250 to 100 infected inhabitants.

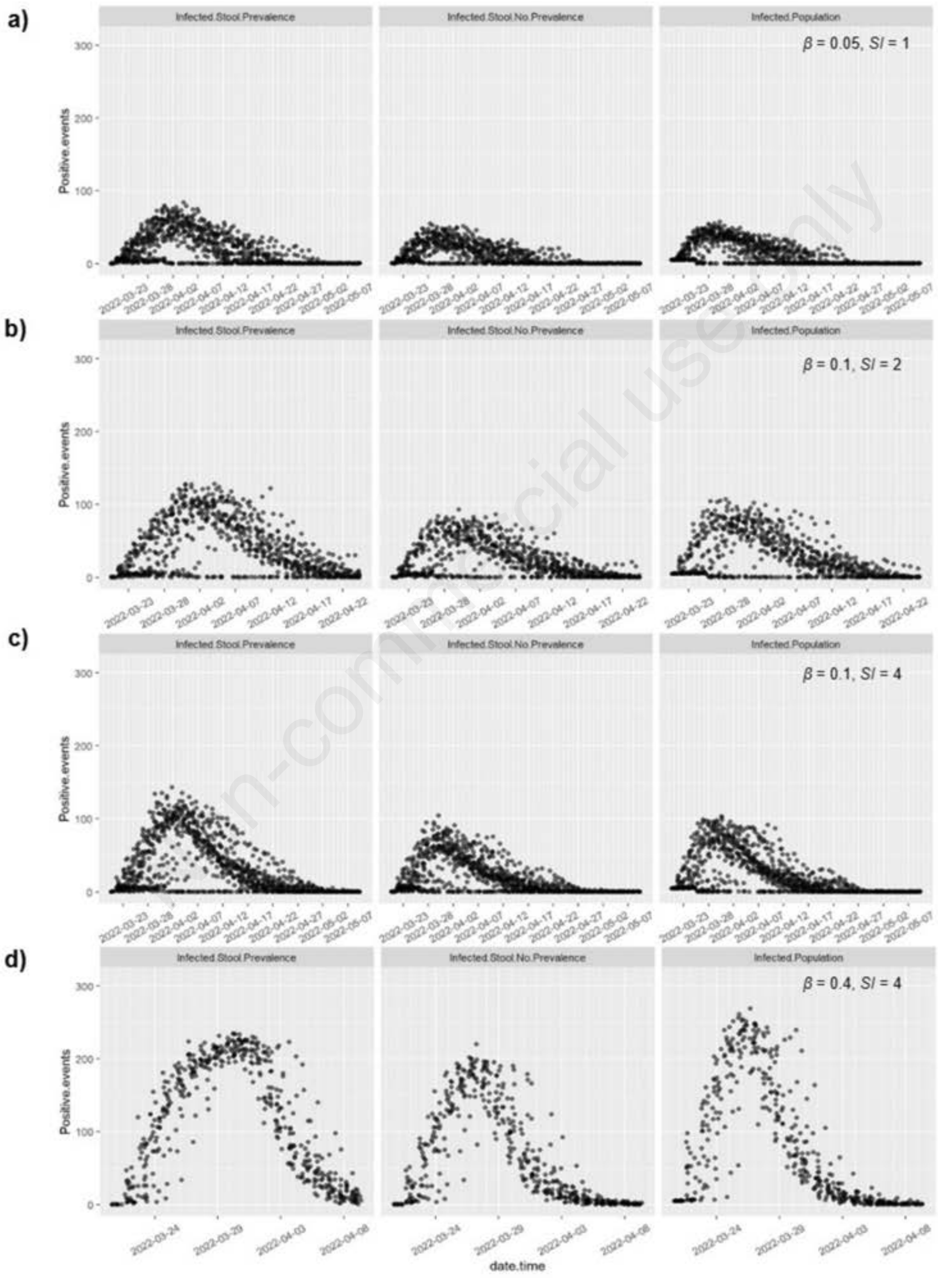

Figure 3. Epidemic curves of simulated outbreaks for the population and infected stool. The stool columns differentiate between infected stool with and without considering whether the recovered population continues to produce infected stool. Rows a, b, c, and d represent four simulations with different combinations of transmission probabilities (β) and the maximum number of possible inhabitants that can be infected (SI). Each scenario is run 25 times to ensure stable results.

Mobility and COVID-19 spread

Figure 4 shows the pattern of inhabitants' mobility during the outbreak. As inhabitants stay home when infected, the number of people at home increases. At the peak, we observe a decrease in mobility of approximately 60 infected agents (1,660 agents at home versus 1,600 at the start and end of the outbreak). After the peak, mobility increases as inhabitants recover, leading to lower individual counts at home. The synchrony between Figures 2 and 4 demonstrates the consistency of the interactions between the sub-models for the outbreak and inhabitants' mobility. This interaction forms the basis for the subsequent production of infected wastewater.

Sewer infected wastewater

Figure 5 shows the simulated infected wastewater particles at sewage maintenance holes at 1-day resolution. The direction of the sewage flow can be explored in the supplementary material in the input data section. The map series consists of 16 days during the main period of the outbreak with 24-hour intervals using disease variables $\beta = 0.4$ and SI = 4. Each timestamp shows the aggregated events from individual agent actions. The epidemic curve of infected stool production (Figure 3d) matches the daily increase of infected wastewater particles shown in the map series (Figure 5). Both figures 3 d and 5 synchronize between 26 March and 1 April illustrating the spatiotemporal dynamics of infected wastewater particles. The results from Figure 6, here shown for a single day with 6- and 60-minute intervals, illustrate the spatiotemporal heterogeneity of infected wastewater particles. The 6-minute time stamps in Figure 6 b preserve information from individual agent actions and reveal the intermittent infected wastewater that cannot be seen in Figure 6 a. The counts of infected wastewater particles peaked at 30 to 60 infected wastewater events between 09:00 and 10:00. After 10:30, there was a substantial decrease in infected wastewater. The map series from Figure 6.a differs from Figure 6.b by using hourly intervals between 8:00 and 11:00 instead of the 6-minute intervals, which shows that the maximum number of infected wastewater events occurs between 9:00 and 10:00 A.M. with 500 and 600 events from the total of the 25 simulations. Although the hourly intervals in Figure 6 a represent spatiotemporal heterogeneity of the sewage flow of infected events, the heterogeneity is considerably reduced compared to Figure 6.b.

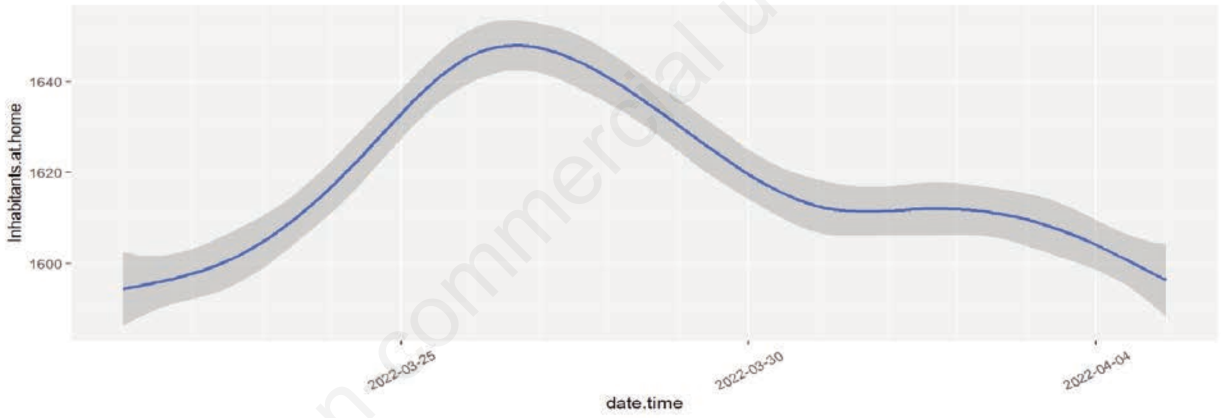

Figure 4. Mobility pattern of the count of inhabitants at home during an outbreak. The mobility pattern shows the increase of inhabitants remaining at home during the days of the outbreak (2022-03-23 to 2022-03-31), which synchronizes with Figure 2.

Table 3. Output summary.

Integrated DMW model	Output description	Brief interpretation of the model integration for COVID-19
COVID-19 outbreak	The epidemic curves with daily positive numbers of COVID-19 population cases and produced stools with and without SARS-CoV-2 prevalence	The added value of the integrated outbreak study is the capability of estimating the number of infected wastewater flushes that the inhabitants generate (which forms the infected stool production)
Mobility and COVID-19	The spatially referenced daily number of infected inhabitants at household locations during the outbreak The time series counts of the inhabitants at households during the outbreak	The added value of the integration between mobility and the disease allows the study of the variation of population mobility during the duration of the outbreak
Infected wastewater	Spatiotemporal maps of the flow of infected wastewater particles as they change across the sewer at multiple resolutions	The added value is the ability to estimate the production of infected wastewater across the sewer and WWTP

DMW, disease-population-mobility-wastewater; WWTP, wastewater treatment plant.

Summary of outputs

Table 3 outlines the integration of different models used for the simulated COVID-19 outbreak, its relationtship with mobility and the dynamics of infected wastewater. Overall, integrating these models offers a more comprehensive understanding of the dynamics of the outbreak and the way the disease evolved. The outbreak module estimates the number of infected individuals and the corresponding infected wastewater from stools, linking disease data with the wastewater modelling, while the mobility-outbreak module analyses the impact of population movements on virus spread by tracking daily infected individuals in households. Finally, the wastewater module provide spatiotemporal maps of the flow of infected wastewater offering insights into wastewater dynamics.

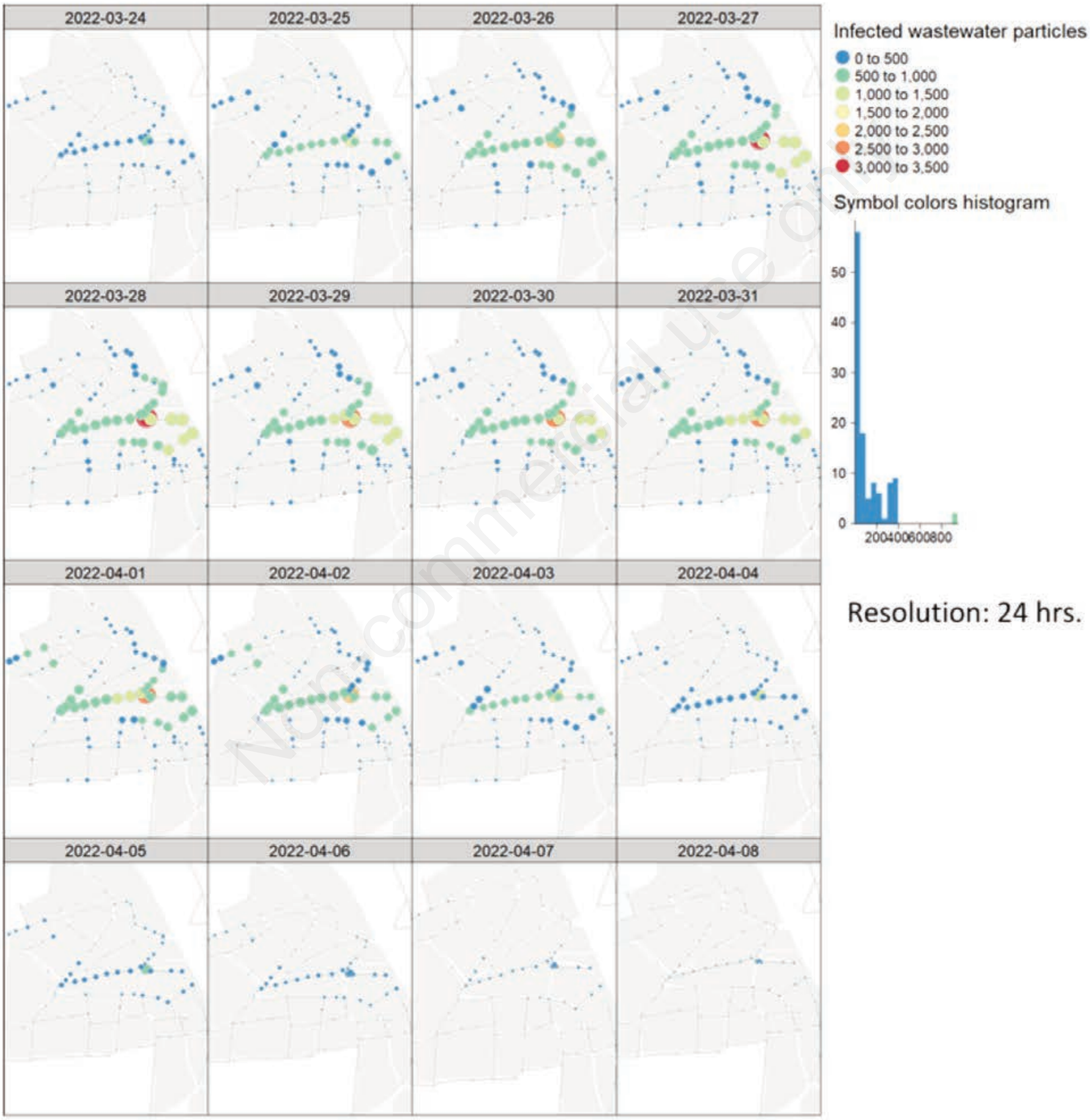

Figure 5. Simulated infected wastewater particles at sewage maintenance holes at a daily resolution. Map series with 24-hour interval during the outbreak period from 25 simulations showing the daily transition of the number of infected particles using disease variables β=0.4 and SI=4. The spatiotemporal heterogeneity distribution of the coloured circles reflects the accumulated flow of events in the main collectors, representing a sewer pattern.

Discussion

The DMW approach demonstrates that the integration of the three sub-models (disease, mobility and wastewater) enables comparison of the number of infected inhabitant agents with the prevalence of a disease in wastewater at different locations within a sewer network. An assessment of the DMW output, as a whole, shows that the main spatiotemporal patterns match and that the individual components are consistent with each other. It further shows that the outbreak pattern outputs of the infected population demonstrate plot shapes similar to normal distributions. Using COVID-19 as a case study, we found the extended prevalence of SARS-CoV-2 in wastewater resulting in a curve with an extended maximum comparable with the literature (Randazzo *et al.*, 2020;

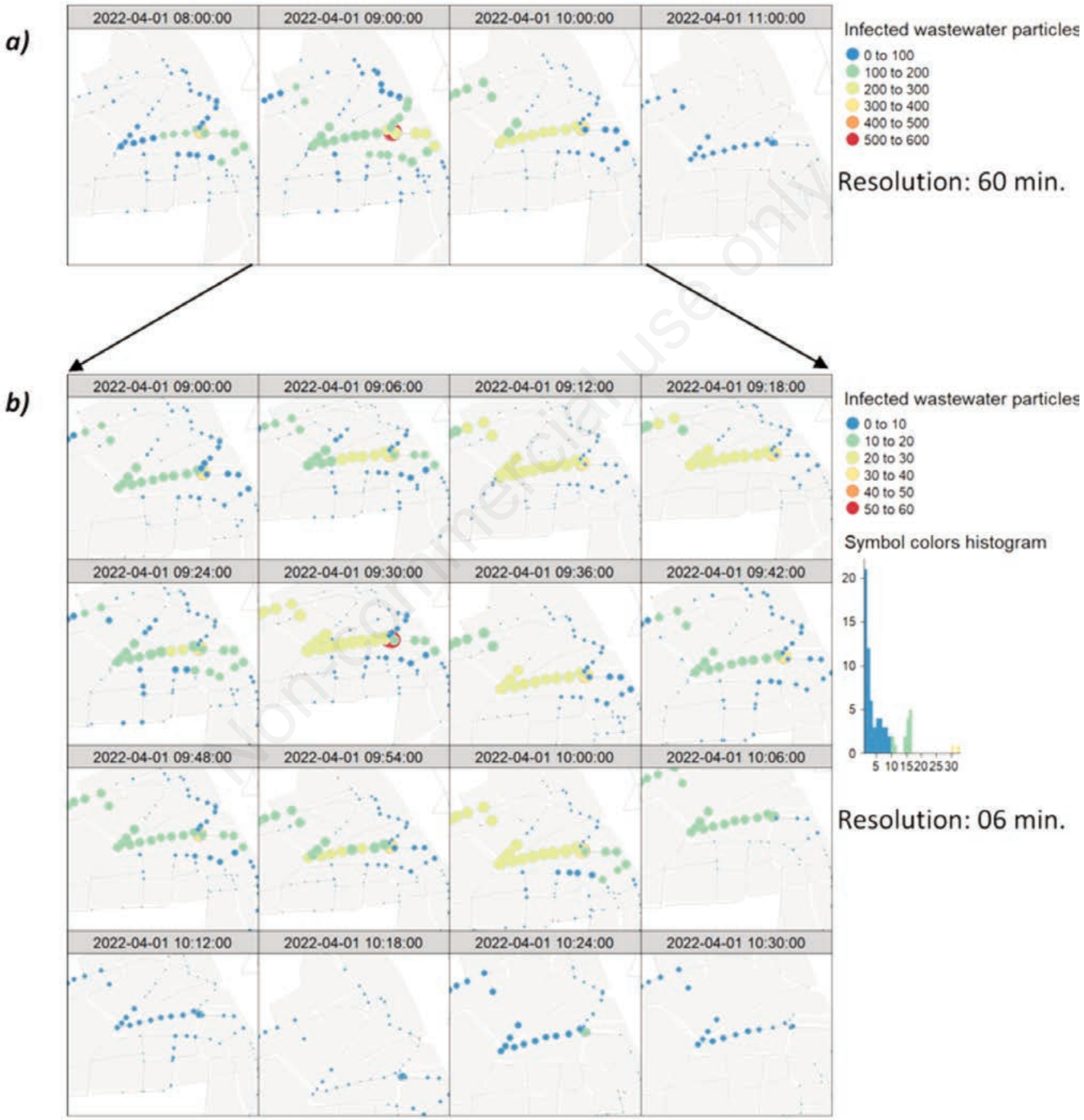

Figure 6. Example of simulated infected wastewater particles at sewage maintenance holes at a daily resolution. Map series with 24-hour interval during the outbreak period from 25 simulations showing the daily transition of the number of infected particles using disease variables β=0.4 and SI=4.

McManus *et al.*, 2023). In addition, the patterns between the mobility dynamics and the spread of the disease found in the literature (Badr *et al.*, 2020; Cartenì *et al.*, 2020) are replicated in the DMW model as the number of inhabitants remaining at home increases, while the spread of the virus increases. The daily sewer resolution matches the epidemic curve pattern, with the infected wastewater across the sewer system replicating the expected pattern following the flow network and accumulating in the collectors as shown in Figure 5.

Modelling at multiple temporal resolutions offers the benefit of better detection of patterns, which is key for ABM validation (Heppenstall *et al.*, 2021). Other studies have confirmed that the temporal and spatial resolutions affect model outputs (Evans & Kelley, 2004; Heppenstall *et al.*, 2021). Depending on the target variable, high or low resolutions may or may not be required for the DMW outputs, e.g., the 1-day resolution is sufficient for the epidemic curve to capture the pattern (Figure 3). However, an hourly resolution must be provided to capture the pattern for population mobility since this resolution excludes population mobility hours (Figure 4). Even more critical, capturing infected wastewater patterns across the sewer requires multiple resolutions. The infected wastewater map series during the outbreak peak demonstrates that the model outputs at different resolutions can differ (Figures 5 and 6). The DMW model required a discrete-event ABM approach to solve two major challenges and to provide pathways for future model integrations. First, the temporal aggregation of agent behavioural rules in the DMW model records individual agent actions in time and space. Second, it overcomes the limited exploration of spatiotemporal heterogeneity at different resolutions thereby facilitating the discovery of hidden patterns, such as the infected wastewater across the sewer. Although there are disease ABMs with high resolutions (Mahdizadeh *et al.*, 2020; Truszkowska *et al.*, 2021), they do not consider individual and disaggregated agent events (or actions) and do not address the two aforementioned challenges, which are key for explaining the spatiotemporal dynamics of infected wastewater. A discrete ABM makes integrating features or sub-models more feasible and makes the DMW useful for studying different spatial and temporal patterns. For instance, the design of the DMW model makes it possible to include rainfall conditions as precipitation time series or integrate hydrological sub-models from similar ABMs (Augustijn *et al.*, 2016). Integrating more target variables, such as gene copies from other pathogens, is possible but requires further research. In general, the DMW model presents alternatives for modelling highly variable or stochastic phenomena in time and space, which require considering more than a single resolution where spatiotemporal heterogeneity is key.

The DMW model has limitations as the current case study focuses on an exploratory model useful to further our understanding of the disease spread linked to the production of infected wastewater. The model was validated for Total Suspended Solids (TSS) with ground true data (De la Paz-Ruíz *et al.*, 2023a), the main indicator for detecting stools in wastewater, while future research will require validating of the outbreak model. However, since the disease outbreak was simulated, strict validation was not needed for this ABM stage (Heppenstall *et al.*, 2021). The assessment of infected wastewater patterns across the sewer also presents an opportunity for future study because of the early state of the art in this field. Complementary to the output verifications, the disease and wastewater integration was analysed by changing the disease variables, demonstrating the behaviour of an outbreak when increasing and decreasing the transmission probabilities of COVID-19. The DMW model is an unsophisticated simulation, and the sub-models are based on relatively simple rules and statistics that can be handy for simplifying the complexities of modelling disease and wastewater.

Conclusions

The DMW model shows a solid integration of disease, mobility and wastewater sub-models, which previous modelling studies have not addressed. It shows consistent patterns between the interactions of the sub-models and has potential for future improvement and applicability. The sophisticated map series with details on spatiotemporal heterogeneity at multiple resolutions differentiates this approach from related models. In addition, the DMW has future applications, e.g., in wastewater epidemiology (and surveillance), for the modelling of pathogens or other substances found in stools and urine that are potentially detectable from wastewater samples. Based on the COVID-19 outbreak, we demonstrated that the integrated model produces trends and patterns compatible with findings as reported in the current literature. The sewer outputs differ between resolutions, highlighting the relevance of modelling at different resolutions for highly variable phenomena. The discrete-event ABM approach can also be beneficial for modelling other diseases or stochastic spatiotemporal phenomena. Our future work will focus on using the integrated model to enhance the sampling methodology used by wastewater surveillance monitoring networks.

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Online supplementary materials

ODD protocol.