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A modular computational framework to foster interdisciplinary integration across the Hub

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Introduction and background

The Hub aims to assess the way in which the configuration of production and distribution networks (PDNs) are influenced by regulatory, social, economic and cultural settings (*structures*), and themselves influence the transmission and evolutionary dynamics of zoonotic health hazards, namely avian influenza viruses, food-borne pathogens and antimicrobial resistance. This requires integration of data and knowledge across biological and social sciences, for which computational modelling is playing a key role in addressing this methodological challenge. A series of interconnected models are currently being developed to simulate (i) the spatial distributions of chicken production (farms) and distribution units (markets, shops, slaughterhouses), (ii) transactions and movements of chickens between units, and (iii) the transmission of health hazards among chickens and from chickens to humans. They will be primarily used to generate hypotheses about the influence of network configurations and chicken management practices on the evolution, dissemination and maintenance of health hazards. These hypotheses will be tested using the data generated by sampling and phylodynamic analyses. Since the models consider explicitly the network actors (e.g. farmers, mobile traders, market vendors), data generated in the fieldwork is being used to calibrate models to realistic scenarios, and also to account for stakeholders' ability to adaptively modify their behaviour in response to changes in social, economic and environmental factors. This makes it then possible to assess the impact of incentives and regulatory changes on network configuration and zoonotic disease risks.

An integrated modelling framework

A modeling framework has been developed, allowing practitioners to simulate the dynamics of in silico PDNs which approximate observed properties of real PDNs. The model explicitly accounts for a variety of actors involved in chicken production and distribution, including farms, middlemen, and stallholders operating in live bird markets, as well as for their practices of these actors. In this context, individual chickens represent a discrete commodity that goes through multiple actors as a result of transporting, trading and marketing practices (Fig. 1). This framework is designed to easily integrate multiple data streams, arising from other research efforts, in order to inform PDN structure and functioning. For example, it can readily adopt fine-grained spatial farm and market distributions generated by point patterns models to instantiate realistic farm demographics (Fig. 2A). Link-tracing studies and surveys of traders' practices also inform the properties of in silico vendors, middlemen and their respective trading patterns. Additionally, the framework allows to simulate transmission of health hazards within and between chicken flocks on top of production and distribution channels. Individual network nodes such as farms, trucks and market stalls, where chickens are stored for varying amounts of time, represent the physical substrate where transmission, either through direct contact or mediated by a contaminated environment, takes place (Fig. 1B). The detailed aspects of this individual-based framework open up to a range of interdisciplinary applications with far-reaching implications for other research teams at the hub. For example, it will be possible to generate transmission chains, which will in turn be used as a benchmark for phylodynamic analysis. Tracking individual chickens' trajectories through PDNs may also help identify transmission hotspots associated with a PDN configuration. These analyses will help social scientists formulate hypotheses about behaviours generating zoonotic disease risks, and lead to a better understanding of the social and economic determinants behind them. Moreover, the explicit modelling of actors embedded in PDNs makes it possible to incorporate features of their decision making. For instance, it will be possible to account for actors' adaptive behavioural responses to certain changes in disease risk, regulatory and socio-economic contexts as informed by social science field studies and economic-derived experiments, and to assess the impact on these responses on the emerging network configuration and the resulting epidemiological outcomes.

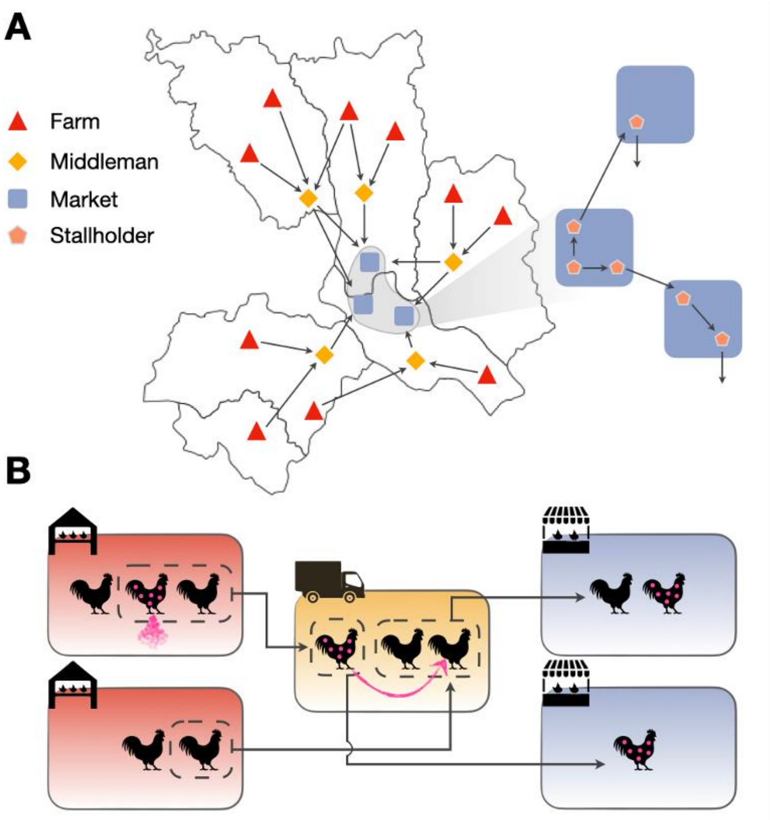

Fig 1: Model schematics. A) The computational model generates a spatially-explicit population of farms (red triangles) and markets (blue squares). Birds flow from farms to markets, with transport being operated by middlemen (yellow diamonds). Within markets, birds are bought and sold multiple times by stallholders (orange symbols) before leaving the system; stallholders can also move between markets. B) The model tracks individual birds' movements and pathogen transmission events. Infected birds can transmit a pathogen to other birds in the same place either i) directly (pink arrow), or ii) indirectly, by shedding infectious particles in the environment. In addition, iii) infected farms can further disseminate a pathogen to neighbouring premises according to their mutual distance. Note that middlemen can pick up

birds from multiple farms and deliver them to multiple markets, increasing mixing opportunities for birds from different geographical areas.

An innovative platform for the exploration of interdisciplinary research hypotheses

The modelling framework developed by the Hub provides significant improvements over existing simulators

- First, it explicitly accounts for a variety of actors, namely farms, middlemen and stallholders, each with its own behavioural pattern and functional role within the PDN.
- Secondly, this is to our knowledge the first framework that allows to simulate a large-scale domestic animal supply chain, while leveraging multiple data sources to inform each step along the chain. Despite being designed for data-intensive approaches, the framework provides a generative algorithm able to explore a wide range of theoretical PDN configurations with different properties. This paves the way for a range of applications, from simply exploring the impact of different network properties and actors' practices on risks of health hazards, to the assessment of intervention strategies modifying the configuration of a PDN.
- Thirdly, compared to other simulators, the Hub's framework explicitly considers individual birds, making it possible to generate individual chicken trajectories within PDNs, as well as generating transmission chains, which could be of value for interdisciplinary integration with phylodynamic modelling and social science studies.
- Finally, the Hub's framework can easily integrate a wide range of epidemic models that might be appropriate for different health hazards. In the context of infectious agents, the model allows to incorporate several assumptions about the life history of pathogens and their hosts, e.g. latency, maternal immunity and disease-induced mortality, as well as multiple pathogen phenotypes and their interactions. This paves the way to investigating outstanding ecological questions that include, for example, the conditions for emergence and amplification of highly-pathogenic avian influenza strains, or the maintenance of resistance phenotypes in PDNs.

State of development – successful PDN generation

A first version of the modelling framework has been successfully implemented and is currently undergoing extensive testing; at the same time, the model is being calibrated against data collected in the context of other research work, with the aim to generate in silico PDNs that are as realistic as possible, i.e. sharing as many empirical features of real PDNs as assessable by available data. Early experiments (Fig. 2) demonstrate that simulations can indeed reproduce fine-scale network properties, such as the distributions of markets visited daily by middlemen (Fig. 2B), and the sizes of stallholders' daily shipments (Fig. 2C), as well as more 'coarse' properties, including the volumes of bird fluxes between any combination of administrative areas (upazilas in Bangladesh) and markets (Fig. 2D).

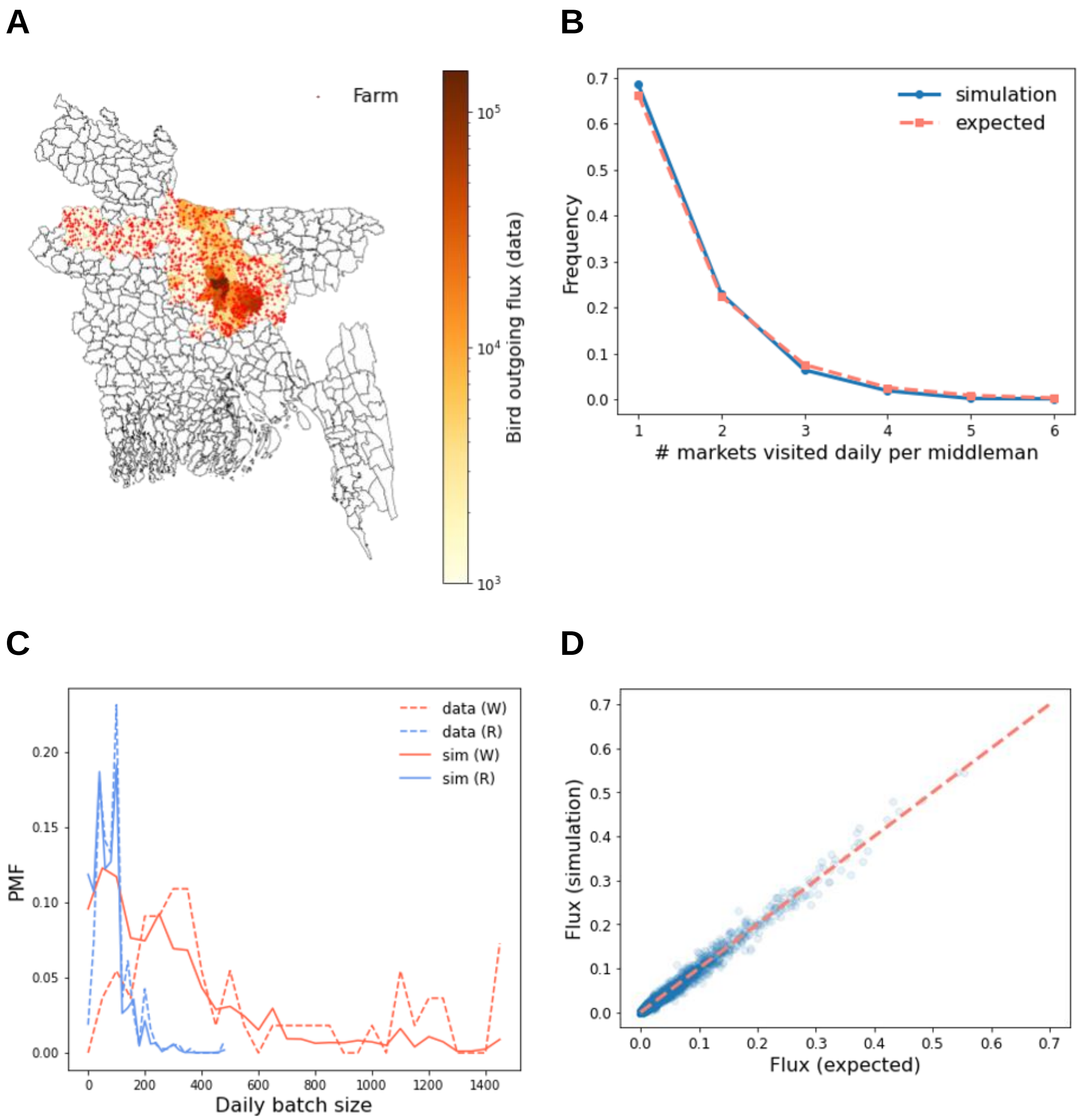

Fig 2: Model calibration. A) Spatial distribution of 1000 farms (red dots) in 100 upazilas (or sub-districts) in Bangladesh supplying the largest amount of broiler chickens to live bird markets in Dhaka. Colour-scale indicates the weekly absolute number of broiler chickens leaving an upazila. B) Distribution of the number of distinct markets visited daily by a single middleman, as obtained from simulations (blue) and from in-market survey data (red). C) Distributions of the daily amounts of bird shipments received by market stallholders as obtained from simulations (solid lines) and from in-market survey data (dashed lines). Red lines correspond to wholesalers, i.e. stallholders selling chickens to other stallholders, whereas blue lines correspond to retailers, who sell only to end-users. D) Individual fluxes from each upazila to each market, scaled by the total flux volume leaving an upazila and scattered against the corresponding expected values.

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