

# Accessing the Impact of the Contact Transmission Network Topology in Ebola Virus Epidemic in Liberia: a Comparative Study using Agent-Based Simulations

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We study the effect of network topology on the dynamics of the Ebola virus disease epidemic that broke out in the Spring of 2014 and swept through the countries of West Africa leaving behind a death toll of more than 11,000 people. Extending an agent-based model that we have developed and which has proven to approximate and forecast quite well the evolution of the epidemic in Liberia and Sierra Leone, we study the influence of two types of networks that are used to approximate the underlying social transmission network: Newman-Watts and Albert-Barabasi. Here, we focused on the case of Liberia. Key epidemiological parameters, namely, the mean incubation period, the time from the onset of symptoms to death, and the time from the onset of symptoms to recovery were taken to be the reported by the WHO response team, while the per-contact transmission probability, the case fatality ratio and the parameter used for the construction of the corresponding graphs were fitted to the time-series of total cases and deaths reported by WHO from May 27, 2014 to December 22, 2014. Our analysis shows that the agent-based simulations on Newman-Watts topology structures perform adequately in approximating the reported evolution for a wide range of probabilities of adding short-cuts, while with the Albert-Barabasi topology perform less efficiently.

## 1. Introduction

For the last years, the Ebola outbreak devastated West African countries with a total of 28,603 cases and a total death toll of more than 11,300 people (CDC, 2016). An epidemic alert was announced in March, 2014 when authorities announced 49 cases and 29 deaths in Guinea (WHO, 2014). Liberia, Sierra Leone and Guinea suffered the most among other countries. The spread of the disease was facilitated by the limited public health infrastructure and poverty. Just before the outbreak, these countries had a ratio of only 1-2 physicians per nearly 100,000 population (WHO, 2015). The World Health Organization (WHO) declared Liberia free of the epidemic in May 2015, Sierra Leone in November 2015 and Guinea in December of 2015 (WHO, 2016).

During the period of the outbreak, scientists from multidisciplinary fields worldwide have teamed up in a race against time, joining their efforts to help containing the epidemic. Towards this aim several studies integrating epidemiological modeling with almost daily surveillance data for the spread as reported by WHO and CDC were published for accessing the outbreak severity and predicting its future evolution. Mathematical models ranged from mean-field deterministic to stochastic and agent-based models on networks (Fisman et al., 2014; Gomes et al., 2014; Kiskowski, 2014; Siettos et al., 2015, 2016; Stadler et al., 2014; Towers et al., 2014; Volz and Pond, 2014). In previous works (Siettos et al., 2015, 2016) we have developed a detailed agent-based model that evolves on small-world networks to provide estimations of key epidemic parameters including the mean time from the onset of symptoms to death or to recovery, the case fatality rate and the per-contact

transmission probability. Using the agent-based simulator, we also estimate the expected effective reproductive number  $R_e$ . Estimations of the structure the underlying transmission small-world network were also provided. Bridging of the detailed individualistic simulations with the emergent macroscopic dynamics (case counts reported by WHO) was achieved using the Equation-Free framework for multiscale computations (Kevrekidis et al., 2004, 2003). Our approach has proven to provide accurate predictions for the evolution of the epidemic in Sierra Leone and Liberia succeeding to forecast when the epidemic would fade out ahead of time (Siettos et al., 2015, 2016).

Here we extend our modeling framework and analysis by assessing the impact of the social transmission network to the approximation quality of the model. For this purpose we use two different algorithms that create in general networks with small-world characteristics as these pertain to the topology of social networks. In particular we simulated the underlying contact transmission network with the Newman-Watts (Newman and Watts, 1999) and the Albert-Barabasi (Albert and Barabási, 2002) algorithms. We employed the concept of the Equation-Free approach to fit the epidemic parameters of the model and the parameter(s) that control the construction of the corresponding networks to the cases reported by WHO and CDC (CDC, 2016). The approximation quality was assessed from simulations in the period May 27, 2014 to December 21, 2014. Fitted values of the network and model parameters as well as estimates of the effective reproductive ratio were computed in sequences of succeeded time intervals of 70 days. The trust-region-reflective approach for nonlinear minimization was implemented for parameter estimation (Coleman and Li, 1996). The proposed approach for multi-scale computations of (re)emergent epidemics can be integrated in a "holistic" risk assessment model of natural disasters and natural hazards (Marzo et al., 2012; Panico et al., 2015). Due to inadequate health infrastructure and absolute impoverishment of the population, large wildfires, big industrial accidents and earthquakes can initiate outbreaks of (re)emerging epidemics, as for example happened in Haiti after the earthquake of January 12th, 2010.

## 2. Methodology

### 2.1 The agent-based model

Our agent-based model is the one presented in (Siettos et al., 2015, 2016) and it has been proven to forecast successfully the evolution of the Ebola Epidemic in both Liberia and Sierra Leone. Agents are categorized in five discrete states: *Susceptible* ( $S$ ), *Exposed* ( $E$ ), *Infected* ( $I$ ), *Dead of the disease but not yet buried* ( $D_I$ ), and *Dead of the disease and safely buried* ( $D_b$ ). Hence, the state space can be represented by  $Y(\mathbf{V})$ , where  $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$  is the set of the states of individual  $v_k$ . The dynamics evolve on a network which represents the underlying social/ contact transmission network according to the following *non-Markov random process*:

$$p(Y_{v_k}(t+1) = D_b | Y_{v_k}(t) = D_I) = 1 \quad (1)$$

$$p(Y_{v_k}(t+1) = E | Y_{v_l}(t) = I, Y_{v_l}(t) = D_I) = p_{s \rightarrow E}, v_l \in \mathfrak{R}_{v_k} \quad (2)$$

$$p(Y_{v_k}(t+1) = I | Y_{v_k}(t) = E) = p_{E \rightarrow I} \quad (3)$$

$$p(Y_{v_k}(t+1) = D_I | Y_{v_k}(t) = I) = p_{I \rightarrow D} \quad (4)$$

$$p(Y_{v_k}(t+1) = R | Y_{v_k}(t) = I) = p_{I \rightarrow R} \quad (5)$$

The parameter  $p_{s \rightarrow E}$  denotes the per infected contact transmission probability,  $p_{E \rightarrow I}$ , is the probability that reflects the inverse of the incubation period,  $p_{I \rightarrow D}$  is the probability representing the inverse of the time from symptoms onset to death,  $p_{I \rightarrow R}$  is the probability corresponding to the inverse of the recovery period, and,  $p_{D/I}$ , is the ratio of deaths to the infected population. The values of these parameters as reported by the Who Ebola Response Team (WHO Ebola Response Team, 2014) for Liberia are as follows: incubation period 9.4 days, time from the onset of symptoms to death 7.4 days, and, time from the onset of symptoms to recovery 15.4 days.

## 2.2 The contact transmission networks

Here we considered two types of complex networks, namely, Newman-Watts (Newman and Watts, 1999) small-world and the Albert-Barabasi (Albert and Barabási, 2002) that we briefly describe at next.

### *Newman-Watts network*

The construction algorithm resembles that of the celebrated Watts-Strogatz network model (Watts and Strogatz, 1998), but without switching edges from the underlying ring lattice: short-cut edges are just added between pairs of nodes with a probability  $p$ . Hence, the algorithm starts with a one-dimensional ring network with  $k$  local-nearest neighbors per node and with a probability  $p$  a link is added between two nodes. Thus, the resulting mean number of additional shortcuts is  $p_{rw} k N$ , and the mean total degree of the network is  $2k N(1 + p_{rw})$ . Note that for  $p$  relatively small the network exhibits small world characteristics while for  $p$  close to 1 the network resembles a random graph.

### *Albert and Barabási network*

The network is created by starting from an initial network with  $m_0$  connected nodes and a new node is connected to the existing graph at each iteration. Each new node is linked with  $m < m_0$  nodes with a probability  $p(k_i) = \frac{k_i}{\sum_j k_j}$  where  $k_j$  is the degree of the  $j$ -th node. This procedure is called preferential

attachment. The distribution of degrees after  $t$  iteration is given by  $P(k) = \frac{2mt}{m_0 + t} \frac{1}{k^3}$ ; for  $t \rightarrow +\infty$  we

have  $P(k) \sim 2m^2 k^{-\gamma}$ ,  $\gamma = 3$ .

## 2.3 Data Fitting

Here we aimed at computing the best estimates for the per-contact transmission probability  $p_{s \rightarrow E}$ , the case fatality rate  $p_{DI}$ , as well as for the networks parameters that control the corresponding underlying topology: the probability  $p$  in the Newman-Watts graph and the parameter  $m$  of the Albert-Barabasi scale-free network ( $m_0$  was set equal to 8). For the Newman-Watts graph we set initial guesses that initialize the network structure (a) close to the ring network with 6 neighbors  $p \ll 1$ , and (b) close to the random structure,  $p \sim 1$ . Regarding the choice of the epidemiological parameters, we note that the per-contact transmission probability  $p_{s \rightarrow E}$  is not directly measurable as other epidemic parameters, while the reported by WHO case fatality rate in the case of the Ebola epidemic is characterized by uncertainty as it is considered highly underreported. Parameter estimates were computed based on the reported time series of the official case counts from the CDC (CDC, 2016). The model parameters were fitted to the reported data coupling a trust-region-reflective approach for nonlinear minimization, implemented for parameter estimation (Coleman and Li, 1996) with the Equation-Free approach (Kevrekidis et al., 2004, 2003; Siettos et al., 2015). The main assumption is that the emergent dynamics can be effectively described by the zero-order moments of the evolving distributions, i.e. the expected values of  $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ . Upon convergence, the effective reproductive ratio  $R_e$ , defined as the average number of secondary infections produced by a typical infective person, was also computed directly from the agent-based simulations.

## 3. Simulation Results

Due to the limitations of computational resources in terms of time (and memory) the number of agents was set to 2 million, that is the half of the actual population of Liberia, based on the demographics reported by the United Nations (UN) (United Nations, 2015). It is noted that the total number of 2 million nodes is already high compared to the number of total cases (of the order of 8,000) and therefore significant differences would not

Table 1: Estimated epidemiological and network parameters for the Ebola epidemic in Liberia (initial guess  $p = 0.02$ , lower limit  $p_L = 0.01$  and upper limit  $p_U = 0.2$ ).

Period	Newman-Watts Network (initial guess $p = 0.02$ )	Mean	95% CI
(May 27- September 8)	network's probability, $p$	0.17	0.16-0.18
	Per-Contact Transmission Probability	0.14	0.13-0.15
	Case Fatality Rate (%)	83	81-85
	$R_e$	6.1	2.3-16.0
(September 8-December 22)	network's probability, $p$	0.18	0.16-0.20
	Per-Contact Transmission Probability	0.086	0.083-0.088
	Case Fatality Rate (%)	38	37-40
	$R_e$	4.9	3.8-5.8

Table 2: Estimated epidemiological and network parameters for the Ebola epidemic in Liberia (initial guess of  $p = 0.5$ , lower limit  $p_L = 0.05$  and upper limit  $p_U = 0.95$ ).

Period	Newman-Watts Network (initial guess $p = 0.5$ )	Mean	95% CI
(May 27- September 8)	network's probability, $p$	0.52	0.50-0.53
	Per-Contact Transmission Probability	0.072	0.071-0.073
	Case Fatality Rate (%)	70	68-72
	$R_e$	3.8	1.3-8.3
(September 8-December 22)	network's probability, $p$	0.44	0.43-0.45
	Per-Contact Transmission Probability	0.030	0.029-0.031
	Case Fatality Rate (%)	35	33-37
	$R_e$	2.0	1.8-2.4

Table 3: Estimated epidemiological and network parameters for the Ebola epidemic in Liberia (initial guess of  $p = 0.9$ , lower limit  $p_L = 0.8$  and upper limit  $p_U = 1$ ).

Period	Newman-Watts Network (initial guess $p = 0.95$ )	Mean	95% CI
(May 27- September 8)	network's probability, $p$	0.90	0.89-0.91
	Per-Contact Transmission Probability	0.050	0.048-0.52
	Case Fatality Rate (%)	71	70-72
	$R_e$	3.07	0.75-6.2
(September 8-December 22)	network's probability, $p$	0.83	0.82-0.85
	Per-Contact Transmission Probability	0.019	0.017-0.020
	Case Fatality Rate (%)	34	33-35
	$R_e$	1.5	1.2-1.7

Table 4: Estimated epidemiological and network parameters for the Ebola epidemic in Liberia. The contact transmission network is approximated with an Albert-Barabasi graph.

Period	Albert-Barabasi Network	Mean	95% CI
(May 27- September 8)	$m$	2	-
	Per-Contact Transmission Probability	0.024	0.023-0.025
	Case Fatality Rate (%)	74	72-75
	$R_e$	0.43	0.1-1.91
(September 8-December 22)	$m$	2	-
	Per-Contact Transmission Probability	0.021	0.013-0.028
	Case Fatality Rate (%)	67	61-72
	$R_e$	0.38	0.29-0.47

be expected if the actual demographics were used. Simulations were performed using May 27, 2014 as an initial date and a time horizon of 30 weeks; thus the last date was December 22, 2014. Thus, fitted values of the network and model parameters, as well as estimates of the effective reproductive ratio, were computed in

sequences of succeeded time intervals of 15 weeks corresponding to 2 periods (May 27, 2014 – September, 8 2014 and September 8, 2014 – December 22, 2014). The initial conditions for the starting date of May 27, 2014 were calculated on the basis of agent-based simulations from May 27, 2014, i.e. the date on which the first cases were officially reported from WHO: 12 cases and 11 dead. Tables 1-4 show an overview of the estimated epidemiological and network parameters as well as the resulting effective reproductive ratio, with their 95% confidence intervals for the Newman-Watts with the estimation of  $p$  restricted to be within (a) [0.01 0.2] (Table 1), (b) [0.05 0.95] (Table 2), and (c) [0.8 1] (Table 3), and Albert-Barabasi network (Table 4). Figure 1 shows the cumulative numbers of infected and dead predicted by the fitted model for the four network structures compared to the reported cases by WHO, respectively.

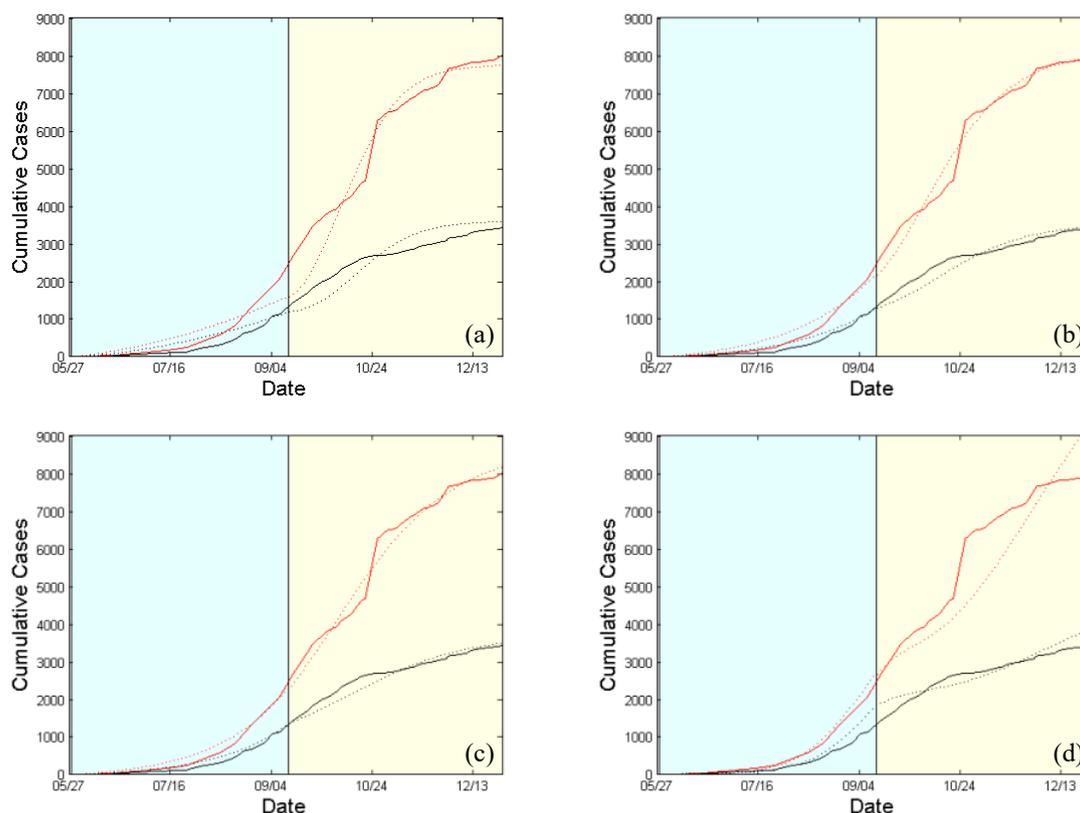


Figure 1. Simulation Results for from May 27 to December 22, 2014. Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 108 days each. For each window, the model parameters are estimated based on the data reported from WHO. (a) Newman-Watts with the estimation of  $p$  restricted to be within (a) [0.01 0.2], (b)  $p$  restricted to be within (a) [0.05 0.95], (b)  $p$  restricted to be within (a) [0.8 1], (d) Albert-Barabasi network.

#### 4. Discussion and Conclusions

Simulations show that the agent-based dynamics network topologies constructed using the Newman-Watts algorithm approximate adequately both the reported from WHO total cases and deaths.

Best fitting is achieved using a probability of adding shorts cuts,  $p$  around 0.5 (also in terms of the reported from other studies mean reproductive numbers (see e.g. ). followed by a  $p$  around 0.9 which indicates that for the particular choice of networks, the underlying contact transmission network simulates a rather random structure. On the other hand the model of preferential attachment performs less efficiently, indicating thus that it is less appropriate for modelling the underlying transmission network.

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