A system dynamics-based simulation experiment for aligning two anthrax progression models and their implications

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Abstract

Two models have been proposed in the literature to describe anthrax progression - the first is referred to as Compartment-B model, which has 22 states, and the other is called Incubation–Prodromal–Fulminant (IPF) model, which has 9 states. How do these two models differ from each other in terms of the indicators considered important by policy or decision makers? Does one always outperform the other based on key performance measures? This paper describes our experience of aligning these two models in the context of anthrax attack. We first develop two simulation models using system dynamics to integrate the key indicators of emergency response, such as treatment rate, detection time, and treatment capacity. We then propose the process of model alignment and examine a large number of numerical examples to see whether the number of deaths, the stabilization time, and the demand for medicine produced by the two models will be reasonably equivalent. This study indicates that it is important for policy makers to understand the differences and similarities between the two models before making decisions. Furthermore, this research provides insights for scholars that rely on simulation tools for investigating bioterrorism attacks and for policy/decision makers that use these tools.

Keywords: Anthrax attack, Model alignment, Compartment model, Simulations, System dynamics

1 Introduction

Recently, the world has grown increasingly concerned about the threats posed by bio-terrorists. In various bioterrorism attacks, anthrax is often chosen for use [1], and was selected by former Soviet Union and the USA as a core microbe for weaponisation [2]. When a large-scale bioterrorist attack (such as anthrax) happens, it is essential to know the diffusion characteristics in order to improve the ability to handle it [3]. Gregory [4] developed a compartment model that has 21 compartments. Chen [5] established a simple Incubation–Prodromal–Fulminant (IPF) model, which has only 9 states. The simple IPF model is a simpler and well-understood model, while the compartment model is complex one, and is difficult to apply in the actual cases. As a result, whether the IPF model can describe the anthrax diffusion rule and whether it can replace the compartment model in coping with an anthrax attack is a research problem and has not been addressed in the literature.

Model alignment [6-7], also referred to as "docking", is the comparison of two computational models to see if they can produce equivalent results. System dynamics (SD) is an analytical modelling approach [8-10], and it deals with the broad behaviour of the system and how it influences its own evolution into the future. We modify the compartment model to include 22 compartments, which are referred to as the "compartment-B model" (B), and we rework the IPF model as "simple IPF model" (IPF). In this paper, our purpose is to demonstrate how to examine the general equivalence between the compartment model and the simple IPF model based on simulated anthrax attacks, and obtain implications from aligning these two models.

The remainder of this paper is organized as follows. Background information about the two models is given in Section 2. The comparison of the two modes and the results are given in Section 3. Finally, conclusions and future research are summarized in Section 4.

2 The Compartment-B and Simple IPF Models based on System Dynamics

2.1 THE COMPARTMENT-B MODEL BASED ON SYSTEM DYNAMICS

When an anthrax attack occurs, the population in that area is divided into mutually exclusive and collectively exhaustive compartments, and there are three disease stages: incubation, prodromal, and fulminant. In the incubation stage, an individual is infected with anthrax but is asymptomatic. The prodromal stage is when the disease is symptomatic with flu like syndrome. The fulminant stage is when the disease is severely symptomatic and is characterized by respiratory distress and followed by death within 24 to 48 hours. There are four categories of awareness and treatment: unaware of

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exposure, aware of exposure but not receiving prophylaxis or treatment, in prophylaxis, and in treatment. According to the three stages and four categories, any individual can fall into one of the 22 compartments (or states). Note that the first 21 states are established by the study of [4] and the last state – the 22nd state (death) is added in this paper. Individuals move between compartments according to a set of transition rates. We assume that R_{itoj} (i, $j \in (1, 2, 3, 22)$) is the transition rate from compartment i to j, the value of which can be shown in Table 1 [8-9]. In addition, the rate of entry into prophylaxis is assumed to be α_1, and the rate into treatment is assumed as β_1.

TABLE 1 All of the transition rates in the compartment model

Rate	Value	Rate	Value	Rate	Value
R1to4	0.014	R8to10	0.022	R16to17	0.00005
R2to5	0.014	R9to11	0.022	R6to22	1
R3to6	0.021	R13to14	0.024	R10to22	0.968
R19to20	0.021	R7to17	0.002	R11to22	0.968
R1to2	0.012	R8to17	0.0004	R12to22	0.968
R4to5	0.012	R9to17	0.0003	R14to22	0.968
R7to8	0.012	R13to17	0.00005	R15to22	0.968
R2to3	0.028	R14to17	0.00005	R16to22	0.968
R5to6	0.022	R15to17	0.00005		

According to the anthrax progression rule, the simulation model can be shown below:

$$\begin{cases} X_i(t+1) = X_i(t) + \sum_{j=1}^{22} R_{jtoi} X_j(t) - \sum_{i=1}^{22} R_{itoj} X_i(t) \quad i = 1,2,3,...,22 \\ DP_1(t) = \alpha_1 * (X_4(t) * DPi + X_5(t) * DPp + X_6(t) * DPf + X_{20}(t) * DPi) * DPP \\ DT_1(t) = \beta_1 * (X_5(t) * DPp + X_6(t) * DPf + X_8(t) * DPp + X_9(t) * DPp + \\ X_{10}(t) * DPf + X_{11}(t) * DPf + X_{12}(t) * DPf) * DTT \end{cases} . \quad (1)$$

In the above equations, $X_i(t)$ is the number of people in stage i at time t. DP_1 (t) are denoted as the demand of medicine during prophylaxis, and DT_1 (t) are during treatment. *DPi*, *DPp*, and *DPf* represent a person's length of treatment in incubation, prodromal, and fulminant stages, respectively, *DPP* is the daily amount of medicine needed for treating one person during the prophylaxis period, and *DTT* are during the treatment period.

2.2 THE SIMPLE IPF MODEL BASED ON SYSTEM DYNAMICS

According to [4], the total population exposed to anthrax spores is divided into nine states, which are described as follows: E (exposed but not yet infected), I (incubation), P (prodromal), F (fulminant), IT (incubation with treatment), PT (prodromal with treatment), FT (fulminant with treatment), R (population that recover), and D (population that die). We can calculate the transition rate from the incubation to prodromal stage (*Tip*), from prodromal to fulminant stage (*Tpf*), and from fulminant to death stage (*Tpd*), and these are 0.012, 0.028, and 0.083[9-10]. The transition rate from the incubation, prodromal and fulminant stages to the recovery stage, named as *Tir*, *Tpr*, and *Tfr*, respectively, is set equal to zero [11]. Based on the results published in [10], the recover rate from incubation (*Titr*), prodromal (*Tptr*), and fulminant stage (*Tftr*) are 1, 0.14, and 0.032. In addition, we define the transmit rate from the prophylaxis, prodromal and fulminant stages to the treatment stage are α_2, β_{2p} and β_{2f}, respectively, and the amount of medicine needed for prophylaxis and treatment are DP_2 (t) and DT_2 (t). Hence, we can establish the equations as follows:

$$\begin{cases} IT(t+1) = IT(t) + Tiit * I(t) - (Titpt + Titr) * IT(t) \\ P(t+1) = P(t) + Tip * I(t) - (Tppt + Tpf + Tpr) * P(t) \\ I(t+1) = I(t) + E * Tei - (Tip + Tir + Tiit) * I(t) \\ PT(t+1) = PT(t) + Tppt * P(t) + Titpt * IT(t) - (Tptft + Tptr) * PT(t) \\ F(t+1) = F(t) + Tpf * P(t) - (Tfpt + Tfd + Tfr) * F(t) \\ FT(t+1) = FT(t) + Tpft * F(t) + Tptft * PT(t) - (Tftd + Tftr) * FT(t) \\ D(t+1) = D(t) + Tfd * F(t) + Tftd * FT(t) \\ R(t+1) = R(t) + Tir * I(t) + Titr * IT(t) + Tpr * P(t) + Tptr * PT(t) + Tfr * F(t) + Tftr * FT(t) \\ DP_2(t) = \alpha_2 * I(t) * DPi * DPP \\ DT_2(t) = (\beta_{2p} * P(t) * DPp + \beta_{2f} * F(t) * DPf) * DTT \end{cases} . \quad (2)$$

2.3 THE PROCESS OF MODEL ALIGNMENT

We align the compartment-B model with the simple IPF model and compare the outputs from both models. To make our comparisons manageable and meaningful, we choose some example values for the following parameters: detection time (t_d) = 0, 48, 120, 240, treatment capacity (V) = 5000, 10000, 20000, α_1, β_1 = 0, 0.4, 0.8, 1, α_2, β_{2p}, β_{2f} = 0, 0.4, 0.8, 1, *S1* = *I* = 100000, 200000, 300000, 500000. In addition, *Dpi* = *DPp* = *Dpf* = 60, *DPP* = 0.2, *DTT* = 0.8[11]. Thus, we can have 192 cases (4 x 3 x 4 x 4) of numerical problems. We align the components of the two models in the 192 numerical cases, and the model is implemented by a system thinking software, iThink 9.0. We define the following parameter, *w*, as the percentage of difference between the two models

$$w = (|IPF - B| / B) * 100\%, \quad (3)$$

where IPF and B represents the output results, such as the number of death and the medical demand for treatment. According to Sterman [7] and Oliva & Sterman [12], the output results in the two models are the cumulative value over the entire time series.

3 Simulation results

In this section, the final outputs of the simulated attack, including death rate, stabilization time, and medical demand over time are presented and discussed.

3.1 DEATH RATE AGAINST TIME

3.1.1 The impact of the treatment rate

Table 2 shows the average number of deaths in the compartment-B and simple IPF models in a simulation scenario when the number of exposed people and the treatment rate change. In Table 2, E represents the exposed people, D is the average number of death, R is the treatment rate, B represents the compartment-B model, and IPF refers to the simple IPF model. Figure 1(a) shows the number of deaths against time with full prophylaxis and treatment, from which we see that about 95,342 people suggested by the compartment-B model would die, whereas only 834 people in the simple IPF model would die. This large difference is due to a time lag between the unaware exposed state and the aware exposed state, which delays many exposed people's timely treatment. If we suppose that all of the unaware exposed people search for treatment, we can arrive at a new plot shown in Figure 1(b), from which we see that the number of deaths suggested by both models is very close.

Table 2 reports the quantities of deaths suggested by both models as well as the percentages of difference when E = 100,000; 200,000; 300,000; 500,000, and R = 0, 0.4, 0.8, 1, respectively. As indicated by Table 2, almost all of the exposed people will die when the treatment rate is 0. When the treatment rate is 0.4, about 8.36% of people in the B model will die, whereas 7.28% of those in the IPF model will do. If the treatment rate is 0.8, then 6.86 % and 1.85% of exposed people in the B and IPF model respectively will die. Interestingly, at the full treatment rate (R = 1), 6.55% of people in the B model will die, but only 0.16% of those in the IPF model will die. Consequently, we conclude that the difference between the two models in terms of number of deaths increases with the treatment rate; especially when the treatment rate increase to 0.8 or even 1, the two models differ significantly.

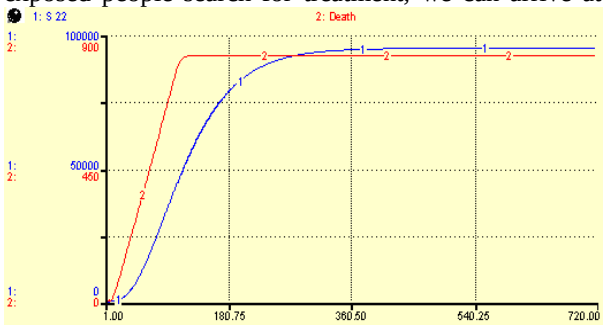

FIGURE 1(a) The Number of Deaths against Time with Full Prophylaxis and Treatment

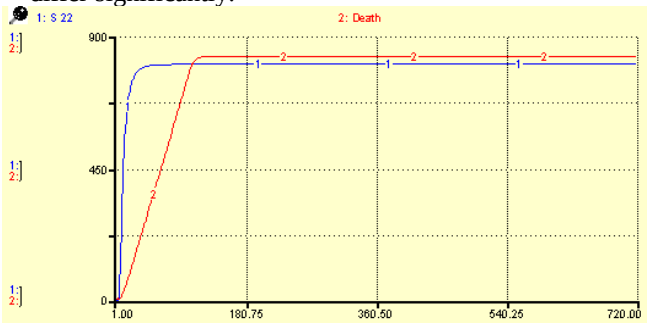

FIGURE 1(b) The Number of Deaths against Time with Full Prophylaxis and Treatment When all of the Unaware Exposed People Search for Treatment

TABLE 2 Average number of death under different treatment rates

	100000			**200000**			**300000**			**500000**		
	B	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*
0	99942	99951	0.01%	199884	199902	0.009%	299827	299853	0.008%	499712	499756	0.009%
0.4	7843	6468	17.53%	16277	13882	14.71%	25304	22190	12.31%	45022	41600	7.6%
0.8	6674	1541	76.91%	13564	3444	76.41%	20660	5688	72.47%	35426	11167	68.47%
1	6550	149	97.93%	13101	317	97.58%	19652	486	97.53%	32753	823	97.49%

3.1.2 The impact of the detection time

We change the detection time to examine its impact on the death rate. As indicated in Table 3, on average 25.54%, 27.78%, 30.83%, 37.56% of the population suggested by the B model, and 25.67%, 26.36%, 27.36%, 29.86% of the same population in the IPF model will die when the anthrax is detected at 0, 12, 24 and 48 hours, respectively. In addition, we observe that the quantities of deaths produced by the two models are very similar if the attack is detected within 12 hours.

TABLE 3 Average number of deaths under different detection times

	100000			**200000**			**300000**			**500000**		
	B	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*
0	25298	25354	0.22%	50894	51097	0.4%	76752	77178	0.56%	129135	130196	0.83%
12	27590	26054	5.57%	55498	52473	5.45%	83440	79229	5.05%	140078	133665	4.58%
24	30671	27085	11.69%	61520	54478	11.45%	92550	82163	11.22%	155114	138568	10.67%
48	37449	29616	20.92%	75004	59496	20.68%	112701	89646	20.46%	188587	150917	19.97%

Under the same assumption, we examine the impact of treatment capacity on the average number of deaths, and the relevant results are reported in Table 4. From this table we can see that the value of *w* are very close, which suggests that increasing treatment capacity is not more effective and cost-effective at the margin to reduce the death rate.

TABLE 4 Average number of death under different treatment capacity

	100000			**200000**			**300000**			**500000**		
	B	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*
5000	30326	27156	10.45%	60987	54832	10.09%	91960	83041	9.70%	154815	141170	8.81%
10000	30327	27007	10.95%	60656	54312	10.46%	91255	81860	10.30%	152941	137730	9.95%
20000	30194	26918	10.85%	60477	54015	10.69%	90867	81260	10.57%	151931	136110	10.41%

3.2 STABILIZATION TIME

We define stabilization time as the number of days elapsed when at least 99% of infected population either die or recover, and we obtain these under the different treatment rate, detection time, and treatment capacity, which are summarized in Table 5. We can see that the values of *w* are very large, implying that the two models are very different in terms of stabilization time when the treatment rate, the detection time and treatment capacity are considered simultaneously. In addition, Table 5 suggests that the stabilization time has a relationship with the treatment rate and the detection time; specifically, if the treatment rate is lower, the stabilization time will be longer. Additionally, if the attack can be detected earlier, the stabilization time will be shorter. However, we cannot find the relationship between the stabilization time and the treatment capacity.

TABLE 5 Stabilization time under different conditions

	100000			**200000**			**300000**			**500000**		
	B	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*	*B*	*IPF*	*w*
0	384	360	6.25%	384	360	6.25%	384	348	9.38%	384	378	1.56%
0.4	240	118	50.83%	244	122	50%	268	130	51.49%	228	160	29.82%
0.8	242	108	55.37%	240	206	14.17%	252	130	48.51%	242	160	33.88%
1	210	94	55.24%	221	120	45.70%	234	124	47.01%	234	140	40.17%
0	212	152	28.30%	210	162	22.86%	228	164	28.07%	176	162	7.95%
12	254	162	36.22%	265	260	1.89%	274	174	36.50%	272	210	22.79%
24	286	174	39.16%	288	184	36.11%	292	188	35.62%	318	212	33.33%
48	324	192	40.74%	326	202	38.08%	344	206	40.12%	322	244	24.22%
5000	272	171	37.13%	271	255	5.90%	282	197	30.14%	273	225	17.58%
10000	265	170	35.85%	274	178	35.04%	287	179	37.63%	263	206	21.67%
20000	270	170	37.04%	271	172	36.53%	285	174	38.95%	281	191	32.03%

3.3 MEDICAL DEMAND AGAINST TIME

When the parameters such as the detection time, treatment rate and exposed people are changed, different average medical demands can be obtained and summarized in Table 6. It can be seen that when the treatment rate is increased to 1, the medicine for treatment in the IPF model reduces almost to 0. Since there are lots of people who aren't exposed but seek prophylaxis, the medicine demand for prophylaxis in the B model is higher than that in the IPF model. In addition, the medical demand for treatment in the B model is higher than that in its counterpart. All in all, the average quantities of medicine are totally different in the two models in all simulation cases.

TABLE 6 Medical Demand under Different Conditions

# of Exposed People	**Treatment Rate**	**Compartment-B model**		**Simple IPF model**		**Comparison**
		Prophylaxis	*Treatment*	*Prophylaxis*	*Treatment*	*w*
100000	0.4	15153881.08	100423.6	280128.8	72214.05	28.09%
100000	0.8	30309525.3	186815	630691.9	65316.81	65.04%
100000	1	37885494.53	220989.8	840000	0	100%
200000	0.4	15181983.34	225798	542529.51	173769.2	23.04%
200000	0.8	30384672.22	392978	1245563.65	157562.7	59.91%
200000	1	37985901.92	441979.5	1680000	0	100%
300000	0.4	15202172.03	372919.62	789662	300201	19.50%
300000	0.8	3086448.41	617196.49	1845563	274992	55.44%
300000	1	38086448.41	662969	2520000	0	100%
500000	0.4	15219257.96	720701.3	1245768.48	612308.99	15.04%
500000	0.8	30587078.94	1115901.04	3004362.63	579089.00	48.11%
500000	1	38287644.53	1104948.81	4200000	0	100%

4 Conclusions

In this paper, we develop a methodology to align two models of simulating disease progression after a biological attack. From this alignment study, we have shown that the average number of deaths and the stabilization time in the simple IPF model are comparable to the compartment-B model to some extent, on the condition that all of the unaware exposed people in the compartment-B model know they are exposed and seek prophylaxis and treatment. But if the detection lag is long and the treatment rate is large, the average number of death people and the stabilization time of the two models will be different. As for the medical demand, the two

models have a different performance because of their different model structures. In addition, the simulation results indicate that the longer detection time delay will result in more deaths, and increasing the treatment capacity is not more effective and cost-effective at the margin for the community.

It is necessary to point out some limitations of this research. Firstly, we can assume that different age group people will use different dose medicine in the two models. Secondly, we can consider that the transition rate from the incubation stage to prodromal stage in the two models followed a lognormal distribution with a mean of 10.95 days and dispersion factor $e^{-0.713}$ [13]. Thirdly, we can validate the two models in the actual case of anthrax attack in order to develop an efficient response and control strategies. All these areas represent our future research directions.

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