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Degradation of Biological Weapons Agents in the Environment: Implications for Terrorism Response

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We investigate the impact on effective terrorism response of the viability degradation of biological weapons agents in the environment. We briefly review the scientific understanding and modeling of agent environmental viability degradation. In general, agent susceptibility to viability loss is greatest for vegetative bacteria, intermediate for viruses, and least for bacterial spores. Survival is greatest in soil and progressively decreases in the following environments: textiles, water, hard surfaces, and air. There is little detailed understanding of loss mechanisms. We analyze the time behavior and sensitivity of four mathematical models that are used to represent environmental viability degradation (the exponential, probability, and first- and second-order catastrophic decay models). The models behave similarly at short times (<30 min for our example case) but diverge to significantly different values at intermediate to long times. Hence, for a release event in which the majority of atmospheric exposure or deposition occurs over very short times, the current response models likely provide a good representation of the hazard. For longer time phenomena, including decontamination, the current model capabilities are likely insufficient. Finally, we implement each model in a simple numerical integration of anthrax dispersion, viability degradation, and dose response. Decay models spanning the current knowledge of airborne degradation result in vastly different predicted hazard areas. This confounds attempts to determine necessary medical and decontamination measures. Hence, the current level of understanding and representation of environmental viability degradation in response models is inadequate to inform appropriate emergency response measures.

1. Introduction

Over the past few decades, numerous estimates have indicated the serious threat of chemical and biological terrorism (*1*−*3*). Biological weapons, in particular, likely pose the most significant terrorism threat. They are relatively easy to produce and could result in deaths comparable to nuclear weapons (*4*). Threat estimates include predictions of hundreds of thousands of deaths resulting from the release of aerosolized anthrax spores in an urban area (*5*). Actual attacks have substantiated the threat of chemical and biological weapons (CBW). In the 1990s, the Japanese cult Aum Shinrikyo released sarin gas both in the city of Matsumoto and in the Tokyo subway (*6*). In 2001, anthrax spores were enclosed in letters sent through the United States mail system (*7*). These attacks resulted in several deaths, numerous hospitalizations, and widespread fear (*8*, *9*). The economic impact associated with these actual attacks and with defense against the threat is also significant. The Henry L. Stimson Center estimates that the Federal Government spent 1.77 billion dollars on defense against weapons of mass destruction terrorism in fiscal year 2002 (*10*). Additionally, decontamination after the 2001 anthrax attacks alone exceeded 100 million dollars (*11*).

Mathematical models are used to estimate the hazard resulting from an actual release of a CBW agent. They are also used to plan for the response to such releases. Response and planning models typically include representations of agent release physics and chemistry, transport and dispersion of the agent in the atmosphere, agent viability decay in the environment, agent deposition on surfaces, and calculation of the resultant hazard. Example hazards include human or animal injury or death and extent of the contaminated area. In this work, we focus on one aspect of response and planning modeling, namely the representation of biological agent viability degradation (or decay) in the environment. Here, we define viability degradation as the injury to or death of the biological agent, causing it to be less harmful. (Our definition does not include physical processes, such as coagulation of agent particles. These result in lowered infectivity but do not injure or kill the agent.) Numerous damaging processes impact biological agent survival in the atmosphere and after deposition on surfaces. These include heating, desiccation, irradiation, and oxidation. The rate of agent death or injury in the environment may have a significant impact on the hazard resulting from a terrorism release. It will certainly affect the level of decontamination needed to ensure that the hazard area is safe to occupy. Therefore, understanding and modeling of environmental viability decay of biological agents is necessary for terrorism response planning.

In this work, we probe the current understanding of degradation of biological weapons agents in the environment and investigate its implications for terrorism response. In Section 2, we summarize the state of the science on biological weapons agent degradation in the environment. Section 3 quantitatively investigates the time behavior of different decay models. We also compare the hazard areas predicted by the use of each model in a release simulation. Finally, Section 4 provides a further discussion of the implications of this work for terrorism emergency response planning.

2. Current State of Knowledge

To determine the state of knowledge on biological agent viability degradation in the environment, we performed an extensive literature search (see Supporting Information). Although this search was not exhaustive, it provides a good representation of the publicly available knowledge in the field. Additional research reports relevant to this paper may be available in the classified or unreferenced literature (i.e. from weapons programs). However, we have confined ourselves to the open literature in the hopes of contributing to the broader public scientific debate on biological terrorism and appropriate response strategies. In this section, we

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provide a general overview of the knowledge available that can inform discussion of viability decay modeling and terrorism response.

Agent Types and Characteristics. There are numerous biological agents that are considered potential terrorist weapons agents. (See the Centers for Disease Control and Prevention Web site for one such list (*12*).)These agents can be categorized into three basic types: spore-forming bacteria, vegetative bacteria (nonspore-forming), and viruses. Biological toxins, including ricin and saxitoxin, are also often included in the biological agent category, although they are not living organisms. Consequently, their behavior in the environment is more similar to chemical weapons agents and is not considered in detail here. Spore-forming bacteria are responsible for diseases including anthrax and Q-fever (a rickettsia with a spore-like form). These bacteria persist in a highly resistant form and, hence, survive dissemination and transport processes more easily. Once inside the host, the spore germinates into a vegetative (growing) state. Other bacteria can be disseminated in their vegetative state, causing such diseases as tularemia and plague. Viruses that are considered potential weapons agents include smallpox, Ebola, and Venezuelan equine encephalitis. Recent reviews provide descriptions of agents, agent types, characteristics, and the medical hazards of specific agents (*13*, *14*).

Measures of Degradation. Several measures are used to describe the hazard that biological agents pose to humans (or animals): survival, viability, and infectivity. Agent *survival* is a nonspecific *general phrase* referring to the ability of a microorganism to initiate growth in an appropriate medium or to initiate disease in a susceptible host. It is used to describe the state of an individual microorganism (cell or virion) or an individual agent particle (which may be a single cell or a group of cells). It is also used to describe the state of a population of cells (or group of particles) as a percentage survival. Agent *viability* refers specifically to the survival of the microorganism *outside a host*, whether it can initiate disease in a particular host. It is a necessary prerequisite for infectivity. *Infectivity* is the capability of a microorganism to invade a host and multiply detectably *in the host*, generally causing disease symptoms. Infectivity includes both agent viability outside the host and the response of the host to a given dose of viable agent (the dose−response relationship). Infectivity is therefore dependent on many host-specific factors, such as immune response (*15*). Since we are interested in the impact of the environment on biological agent survival, we focus on viability degradation for our quantitative analyses. However, in this section we discuss conclusions that can be drawn from all survival studies (in vitro and in vivo).

Degradation Studies. A number of studies have investigated pathogen survival in a variety of environments, including in air, water, sediments, sewage, soil, linens, and on surfaces ((*16*) provides a review). Generalizations from these studies can inform understanding of the survival of potential biological weapons agents. In broad terms, these studies indicate that spores are least sensitive to viability decay in the environment (or under active decontamination processes), vegetative bacteria are most sensitive, and the sensitivity of viruses is intermediate. Studies also indicate that agent survival generally increases in the following progression of environments: in air, on hard surfaces, in water, embedded in textiles, and in soil. Many pathogenic vegetative bacteria only survive for minutes to hours in air, while spores may survive for centuries to millennia in soils. For human pathogens with animal or insect hosts (including plague and the hemorrhagic fever viruses), increased survival may occur if the disease becomes established in these vector reservoirs.

Quantitative studies of airborne biological agent survival have also been conducted. Defense programs at government laboratories have performed much of the work, limiting its availability in the open literature. However, several texts and review articles in the aerobiology field, on airborne survival of surrogate microorganisms and some potential biological weapons agents, provide research results from the defense work (e.g. refs *15*, *17*−*21*). Previous studies have investigated the environmental factors that impact survival. These include many attempts to quantitatively determine the rate of viability or infectivity decay under specific stressor conditions and to develop mechanisms and models that explain the decay rate structure. However, there currently is no detailed quantitative understanding of microorganism viability decay that can be used to develop comprehensive models of degradation as a function of the numerous physical and chemical environmental conditions. Previous research does indicate that temperature, relative humidity, radiation, acidity, oxidants, highly reactive products of ozone and alkenes (historically termed the "open air factor"), and other atmospheric pollutants (e.g. nitrogen dioxide, sulfur dioxide, and formaldehyde) all impact microorganism viability. The mechanisms of inactivation for each of these factors have been studied but are not well understood. Semitheoretical models that have been found to adequately represent airborne and surface viability decay rates under some conditions and for some microorganisms include the exponential decay model, probability decay model (sometimes termed the 'kinetic model') and the catastrophe decay model. These models will each be presented and examined in Section 3. Additional description of each model's development and use can be found elsewhere (*17*−*19*).

Although a few simple models have been developed to explain viability loss due to specific environmental factors, the field is very underdeveloped despite numerous studies. There are differences in experimental design (e.g. differences in agent growth, agent strain, aerosolization technique, collection technique, and viability assay technique) that make comparisons between experiments difficult and, hence, contribute to the lack of coherent understanding and modeling of viability degradation. More importantly, there are some inherent limitations to understanding of viability degradation that have implications for hazard modeling. Fundamentally, biological agents and agent populations are complex living entities. (Viruses are not generally characterized as living while outside the host. Nonetheless, their ability to live in the host is impacted by the environmental conditions prior to entering the host.) The response of biological agents to environmental stressors depends on their hardiness (which is affected by growth conditions and age) and their repair capabilities (e.g. refs *22*−*25* and *16*). A particular assay technique may indicate a decrease in viability due to an environmental stressor. However, if the apparently dead agent is placed in more favorable conditions, it may repair itself and still be infective. Therefore, there are significant hurdles to determining reproducible degradation rates through experimentation. Nonetheless, much further work could be done to understand and to model the complex and dynamic physiological phenomena involved in microorganism survival in the environment. Though, for the purposes of terrorism response and decontamination modeling, this work may be of limited value. At the time of an actual release, detailed knowledge of characteristics impacting agent hardiness (e.g. formulation and growth history) will not likely be known well enough to accurately predict its decay. Complex modeling without the needed input parameters would therefore be suspect.

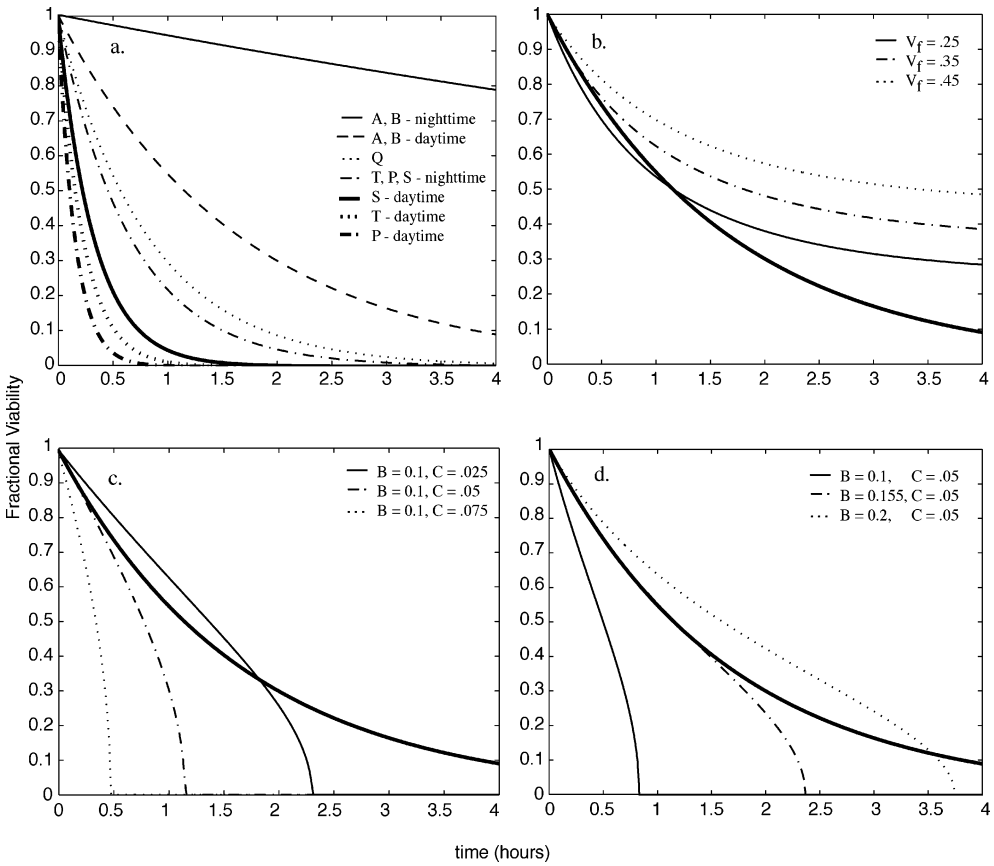

FIGURE 1. Decay models. a) shows exponential decay of several biological weapons agents, based on the HPAC decay rate constants. The letters A, B, Q, T, P, and S indicate the agents responsible for anthrax, botulism, Q-fever, tularemia, plague, and smallpox, respectively. b) shows probability decay for three final viability (V_f) values. c) shows first-order catastrophic decay for three sets of initial crucial moiety concentration (B) and final crucial moiety concentration (C). d) shows second-order catastrophic decay with three sets of initial and final crucial moiety concentrations. In b), c), and d) decay rate constant for all lines is 1.67 $\times$ 10^{-4} s^{-1}, and the thick dark line is for exponential decay.

3. Modeling of Viability Degradation and Hazard

To estimate the hazard resulting from a biological agent release, mathematical models of agent viability degradation in the environment are needed. These degradation representations can be integrated into multiphenomena numerical models that simulate release, transport, and deposition of the agent. Multiphenomena models, such as the Defense Threat Reduction Agency's Hazard Prediction and Assessment Capability (HPAC), are used for real-time terrorism response and pre-event response planning. Mathematical models of agent viability decay are also used to predict and plan for decontamination after a release.

Transformation Capabilities of Current Response Models. There are numerous consequence assessment models that could be used to plan for, or respond to, a terrorist release of a biological weapons agent. The Office of the Federal Coordinator for Meteorology provides a directory and assessment of over 60 models (*26*). Two of the primary operational response models for the Department of Defense and Department of Energy, respectively, are the Hazard Prediction and Assessment Capability and the National Atmospheric Release Advisory Center model (NARAC) (*27*, *28*). These models represent viability loss of a biological agent as exponential decay, during atmospheric transport and after surface deposition. Exponential decay can be represented by the following equation

$$V = e^{-kt} \tag{1}$$

where V is the fractional viability for an agent with the decay constant, k. The fractional viability is the viability at any time, t, divided by the initial ($t = 0$) viability. Decay rate constants are determined experimentally, though the data on which they are based are sparse. HPAC and NARAC also include sinusoidally varying decay rate constants, dependent on the solar zenith angle, to account for the effect of sunlight on decay. The decay rate constant is at a maximum value at solar noon and a minimum value between sunset and sunrise.

Exponential decay is the theoretical representation of loss due to a first-order chemical reaction (e.g. ref *29*). For a population of microbes it assumes that a single lethal event is responsible for death (inactivation) of a member of the population (a cell, spore, or virion) and that the probability of death for any member is equal, random, and constant over time (*24*). Fractional viability following the exponential decay equation is initially one and decays toward zero with time. The decay rate is only sensitive to the decay constant, with V decreasing faster for larger k. Figure 1a shows the exponential decay of several different biological weapons agents using the decay constants found in the HPAC model. Exponential decay has been found to describe inactivation of microbes due to exposure to active disinfectants (physical and chemical) (*30*) and is used ubiquitously as a general equation to represent decay when the details are poorly understood. Thus, it is used to model viability degradation of biological weapons agents in the airborne and surface environments.

Generalized Degradation Formulations, Behavior, and Sensitivity. In addition to the exponential decay model, Cox and co-workers have developed probability and catastrophe

degradation models (e.g. ref *17*). Each contains two components, a reaction kinetics component and a population dynamics component. Both models assume that there is a moiety within a microorganism (e.g. the cell membrane or DNA) that is crucial to the activity (growth or infectivity) of the microorganism. It is this moiety that is detrimentally impacted by a particular environmental stressor. The kinetic component of each model describes the kinetics of the reaction responsible for deactivation of the crucial moiety (e.g. a first- or second-order reaction). The population dynamics component describes how a population of microbes responds to the inactivation of a crucial moiety and how the crucial moiety is distributed in the population. The probability and catastrophe population dynamics components are based on probability and catastrophe theories, respectively (*17*). Here, we formulate generic mathematical expressions for each of these models in order to examine their time behavior and sensitivity. We examine the probability model with first-order reaction kinetics as well as the catastrophe model with first-order and simple second-order (e.g., dimerization) reaction kinetics.

The probability model assumes that the concentration of the crucial moiety is distributed uniformly throughout the agent population. As the crucial moiety concentration in a member decreases, the viability of that member decreases. In practice, first-order reaction kinetics are assumed in conjunction with the probability model. The probability model has been used to represent viability loss due to dehydration as well as other stressors (*17*). The first-order probability decay model can be formulated as

$$V = e^{[AB(e^{-kt}-1)]} \tag{2}$$

where B is the initial crucial moiety concentration and A is a proportionality constant. Figure 1b shows the viability loss using the probability model formulation, assuming the decay constant, k, is equal to the HPAC daytime anthrax spore decay rate (1.67×10^{-4} per second). As seen in the figure, the model is characterized by its approach to an equilibrium (constant) final viability value, $V_f = e^{-AB}$. It is sensitive to both the decay constant, k (not shown), and the final viability value.

The catastrophe model assumes that there is a minimum crucial moiety concentration that results in cell death. Reduction in the moiety concentration below this minimum results in a population "crash". First- and second-order reaction kinetics of moiety concentration decay have been used within the catastrophe model to describe viability loss due to desiccation, temperature, oxygen, and the "open air factor" (*17*). The catastrophe decay model with first- and second-order reaction kinetics can be formulated, respectively, as

$$V = \sqrt{A(Be^{-kt} - C)} \tag{3}$$

$$V = \sqrt{A\left(\frac{B}{1 + ABkt} - C\right)} \tag{4}$$

where C is the minimum crucial moiety concentration that leads to a population "crash". Setting the proportionality constant A to $1/(B-C)$ in both equations yields an initial fractional viability of one. The second-order reaction kinetics formulation above assumes a single reacting species (e.g. a dimerization reaction). Figure 1c,d shows viability decay using the first- and second-order catastrophe model formulations, respectively. Both models are sensitive to the decay constant and the difference between the initial and final moiety concentrations (B and C). The catastrophe models have generally been used to simulate an initial slow decay rate that accelerates (giving a concave down trajectory) and, hence, a quick population "crash" to zero viability.

Comparison of Degradation Models. Figure 1 also provides a comparison of the time behavior of the exponential, probability, and catastrophe models. In order for the models to initially follow similar trajectories, the decay constants must be equivalent. Hence, we have shown curves for equal k (1.67×10^{-4} s^{-1}). Given equal decay constants, the probability model initially follows a path slightly below the exponential decay curve and then crosses at some time

$$\tau_p = \frac{2}{k}\left(1 - \frac{1}{AB}\right) \tag{5}$$

After crossing the exponential curve, the trajectories quickly diverge and the probability line approaches a constant value. The larger the final viability value, the sooner the lines cross and diverge. However, with smaller final viability values the probability trajectory falls further below the exponential trajectory prior to crossing. Hence, there is an optimal final viability value (dependent on the decay constant) for which the probability line stays closest to the exponential line for the longest time. For the decay rate constant used in Figure 1b, this value is 0.35.

The first- and second-order catastrophe models approximately follow the trajectory of the exponential model for early times. However, they do not experience the tailing effects of the exponential and probability models. Instead they approach zero at a quicker rate, experiencing accelerating decay with time. For the first-order catastrophe model (and this decay constant), the line falls below the exponential line for $B \leq 2C$. For $B > 2C$ the catastrophe line starts initially above the exponential line and then crosses it at time

$$\tau_{c1g} = -\frac{1}{k}\ln\left(\frac{C}{B - C}\right) \tag{6}$$

For $B = 2C$, the catastrophe trajectory follows the exponential trajectory for the longest time. Given the same moiety values, the first-order catastrophe model approaches zero more quickly. However, the second-order catastrophe model can follow the exponential model more closely for a longer period of time, given the optimal target moiety values.

Time Scales of Approximate Equivalence. To understand the impact of our current knowledge and representation of biological agent degradation on hazard prediction and, thereby, evaluate the tools we currently use to guide terrorism response, we need to define the conditions under which the differences between the degradation models are significant. To approach this, we have looked at the time scales of approximate equivalence of the basic models available for airborne viability degradation. Specifically, we compare the time scales of approximate equivalence of the probability and catastrophe models to the exponential model. For the probability model, τ_p (given in equation 5) provides a good estimate of the time scale of approximate equivalence with the exponential model, since the trajectories quickly diverge after crossing. For the first-order catastrophe model, the form of the time scale of approximate equivalence with the exponential model depends on the difference between the moiety values. For $B > 2C$, τ_{c1g} (given in equation 6) provides a good estimate of the time scale of approximate equivalence because the lines quickly diverge after crossing. For $B \leq 2C$, the time scale can be determined by finding the time for which the catastrophe line diverges from the exponential line by a small error value, ϵ. This time is

$$\tau_{c1l} = -\frac{1}{k}\ln\left(\epsilon + \frac{B - \sqrt{4\epsilon(B^2 - BC) + (B - 2C)^2}}{2(B - C)}\right) \tag{7}$$

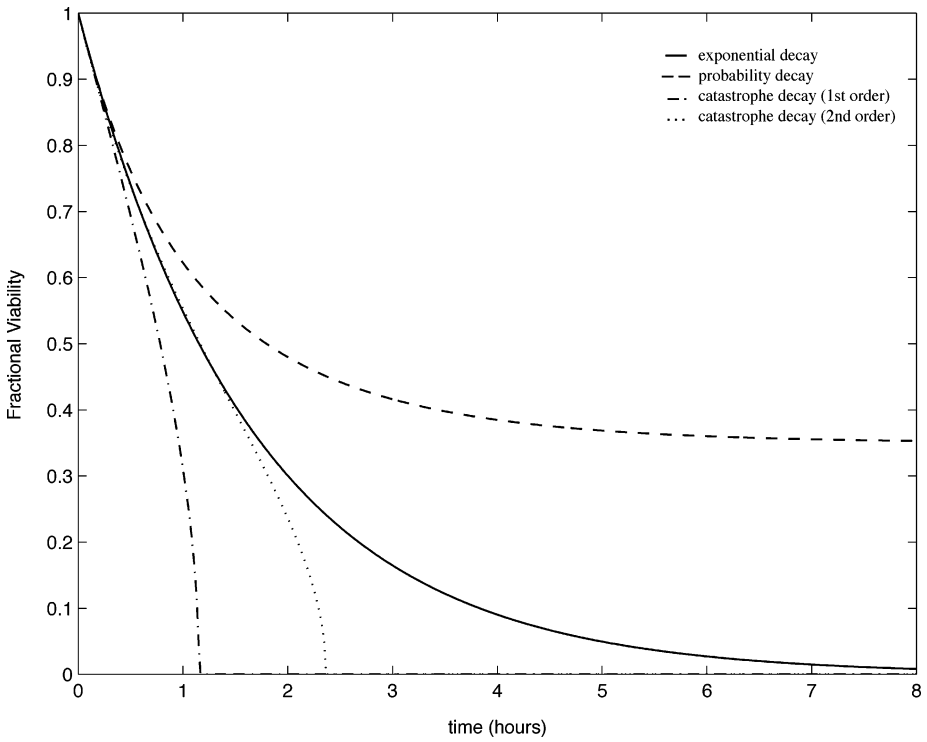

FIGURE 2. Comparison of decay models for 'optimal' constant values. The decay rate constant for all models is 1.67×10^{-4} s^{-1}. The following constants were used: probability model ($V_f = 0.35$), first-order catastrophe model ($B = 0.1$, $C = 0.05$), and second-order catastrophe model ($B = 0.155$, $C = 0.05$). These constants were chosen to maximize the initial trajectory overlap of each model with the exponential model, as discussed in the text.

For the optimal relationship (B=$2C$), this reduces to

$$\tau_{c1o} = -\frac{1}{k}\ln(1 + \epsilon - \sqrt{2\epsilon}) \tag{8}$$

Figure 2 provides a comparison of viability decay for the four models considered here, using the HPAC anthrax spore daytime decay constant. The A and B constants for the probability and catastrophe models were chosen so that the resulting viability values closely approximated the exponential model values for the greatest length of time. We used this approach because most of the decay data upon which the decay models are based are for short times (on the order of minutes to hours). This figure shows that for equivalent decay constants and optimally chosen moiety concentrations, all the models follow the same trajectory for relatively short times (approximately 30 min for this case) but diverge to significantly different values at intermediate times (from 30 min to a few hours for this case). For very long times (more than 8 h for this case), the probability model gives significantly different viability values than the exponential model (which approaches zero), but the catastrophe models give approximately equivalent values to the exponential model (i.e., zero). This suggests that for short time phenomena, a simple exponential degradation model is appropriate. Consequently, for a release event in which the majority of the atmospheric exposure or deposition occurs over short times, the exponential model may be a good approximation to the actual decay and can be used with confidence in response planning. However for intermediate times, the use of the exponential model to represent decay may detrimentally impact response decisions if the actual decay more closely follows the probability or catastrophe curves. This intermediate time period could be within the transport and deposition time for some conditions and species. For phenomena that occur over longer times, such as long-range transport or decontamination (of areas or surfaces), only the probability and exponential model differ significantly. Hence, to mount an effective decontamination, a planner would need to know if the viability approached an equilibrium value (the probability model) or would continue to decay. For example, if an exponential model were representative of the true decay, a cost-effective decontamination strategy could be natural attenuation, while such a strategy would be ineffective if the probability model is more representative. Quantitative values for the short, intermediate, and long time scales depend significantly on the decay constant and the target moiety concentrations and hence are specific to each biological weapons agent and decay mechanism. Unfortunately, there are few data on the appropriate target moiety concentration for each agent, and the values used are generally derived from data with the explicit assumption of a particular decay model. Hence, a universal guide regarding the necessity of improved degradation models for certain response activities (dispersion modeling versus decontamination) cannot be determined without significantly more experimental data.

Effects of the Degradation Representation on the Hazard Resulting from an Airborne Release. To investigate the effects of the degradation model on outcomes for an airborne release, we developed a simple model to estimate the probability of death hazard areas resulting from a release. We compare simulated hazard areas for the four distinct degradation representations with the case of an airborne anthrax release.

Our numerical integration calculates instantaneous downwind airborne concentrations of an agent at breathing height using a simple instantaneous point source Gaussian puff dispersion equation (e.g. ref *31*):

$$\langle c(x,y,t)\rangle = \frac{S}{(2\pi)^{3/2}\sigma_x\sigma_y\sigma_z}\exp\left[-\frac{1}{2}\frac{(x-\bar{u}t)^2}{\sigma_x^{\,2}} - \frac{1}{2}\frac{y^2}{\sigma_y^{\,2}} - \frac{1}{2}\frac{H^2}{\sigma_z^{\,2}}\right] \tag{9}$$

Here c is the concentration at any time, t. The horizontal location is defined by x (downwind distance) and y (crosswind

distance) from the source. The source location is at $x = 0$, $y = 0$, and height H. S is the source strength (in mass or number) released, and $\bar{u}$ is the average wind speed in the downwind direction. The symbols σ_x, σ_y, and σ_z are the downwind, crosswind, and vertical Gaussian dispersion lengths, respectively, which depend on the stability of the atmosphere and increase with distance from the release location. To calculate concentrations, we assumed that horizontal dispersion coefficients in the downwind and crosswind directions were equivalent ($\sigma_x = \sigma_y$) (*32*) and used the Briggs formulations (*33*).

The above equation assumes that the agent does not degrade. To account for environmental viability decay for each type of degradation, equations 1−4 were used to calculate viability as a function of time. The cumulative dose received by a person at any (x, y) location and time, t, was calculated by integrating with time over the product of concentration (assuming no decay), viability, and breathing rate, using the following equation

$$d(x,y,t) = \int_0^t \langle c \rangle V b d\tau \tag{10}$$

where b, the breathing rate, is assumed to be constant with time. To determine the total cumulative dose resulting from a release at any location, equation 10 was integrated until the puff of agent had substantially passed through the entire horizontal domain.

To calculate the hazard area, we determined the cumulative probability of death resulting from a given dose, d, at each horizontal location. To calculate the dose−response relationship, we used the following probit analysis equations

$$p(x,y,t) = \int_{-\infty}^{\zeta} \frac{1}{\sqrt{2\pi}} \exp\left[-\frac{\chi^2}{2}\right] d\chi \tag{11}$$

$$\zeta = m \log_{10}(d/\mathrm{LD}_{50}) \tag{12}$$

where p is the cumulative probability of death in a population. This analysis assumes that the death probability density function is log-normally distributed with dose (with mean log LD_{50} and standard deviation $1/m$). ζ (the probit) standardizes this distribution to a standard normal distribution, $N(0,1)$. LD_{50} is the dose that corresponds to the death of 50% of the population, and m is the probit slope. (See ref *34* for a discussion of probit analysis.)

To investigate the potential effects of viability degradation on response, we applied the model to the case of a daytime anthrax spore release on an urban center. Case conditions were those of Wein and co-workers (*3*). This case represents the release of 10^{15} anthrax spores (1 kg) from a height (H) of 100 m, with wind speed ($\bar{u}$) of 5 m/s and neutral stability conditions. (The Wein et al. case implicitly assumed that all of the anthrax spores were aerosolized in the 1−5 μm size range and hence remain airborne for many hours without settling. A more realistic interpretation of the case parameters would be a 10 kg release where 10% of the spores aerosolized in the 1−5 μm size range. Since this represents the high end of possible biological terrorist attacks, a smaller release is discussed later.) The breathing rate (b) was assumed to be 0.03 m^3/min, representative of a man doing light work. For viability decay, we used the HPAC daytime decay constant for anthrax ($k = 1.67 \times 10^{-4}$ $s^{-1} \cong 1\%$ per minute). Moiety concentration values (given in Figure 2) that maximize the time scales of approximate equivalence were used. Moiety values were optimized in this manner because much of the decay data are for short times. Hence, plausibly representative models should behave similarly at short times. We used an integration time step, $d\tau$, of 10 s and integrated to a final time of 15.5 h. Anthrax spore probit slope and LD_{50} values of 0.7 and 8000, respectively, were used to determine dose response (*35*, *36*).

Figure 3 shows the cumulative death probability contours resulting from this integration. We see from the figure that probability decay results in a larger hazard area than exponential decay, while the catastrophe decay models result in smaller hazard areas. For example the difference between models in the 5% cumulative probability of death hazard area is on the order of hundreds to thousands of square kilometers. For a smaller release (not shown) of 1 g (10^{12} spores) with all other conditions the same, the differences are still significant, with the largest difference between the simulated 5% death hazard areas on the order of 5 square kilometers. For both release cases, these differences could result in very different response decisions. If current response models, which assume exponential decay, are used to predict the consequences of an attack when the actual agent degradation follows probability or catastrophic decay curves, response decisions could be inappropriate. We will discuss here the potential impact on two types of response decisions, medical response and decontamination.

In the event of a biological weapons agent release, medical intervention (e.g. dissemination and administration of antibiotics or vaccines, hospitalization, and isolation) will be necessary. Medical response decisions based on predictions from an incorrect environmental degradation model could be inappropriate. For example, if one uses an exponential model to assess the population at risk and requiring rapid medical treatment, but the actual decay is better represented by a probability model, then at-risk populations could be left untreated until symptoms begin to appear in outlying areas. This could lead to excess death and/or suffering. In addition, the quantity of medical supplies required could be underpredicted with an exponential decay model, because planners would expect a smaller hazard area and, hence, a smaller exposed population. Conversely, if the agent decay actually follows a catastrophe decay curve, too many medical resources could be allocated to the presumed affected areas. This could leave the nation vulnerable to multiple follow-on attacks if the medical stockpiles were overallocated to one city and unavailable to respond to follow-on attacks at a difference location.

Response decisions concerning immediate personal decontamination and longer-term area decontamination would also be negatively impacted by predictions using an incorrect decay model. Public personal decontamination measures and procedures (e.g. the establishment of an immediate response wash-down facility) could be appropriate response strategies after certain biological weapons attacks. The misprediction of hazard areas based on an incorrect decay model would have negative impacts on immediate personal decontamination decisions similar to those for medical response decisions. Potential impacts include increased exposure and death, or, conversely, unnecessary panic, traffic congestion, and unnecessary use of overextended material and human response resources. Additionally, mispredictions from incorrect decay models could negatively impact longer-term decontamination response. For example, initial estimates of the areas that need to be sampled for contamination based on predicted surface deposition (not represented in our simple quantitative model) could lead to a time delay in the determination of contaminated areas and to unnecessary economic expense from inefficient sampling. An area decontamination plan (such as natural attenuation or abandonment) based on the exponential decay model would also be ineffective if agent decay actually followed a probability curve. Conversely, active area and surface decontamination measures could incur significant unnecessary expense if natural attenuation were an appropriate response strategy. Further, distinct environmental conditions (e.g. indoor versus

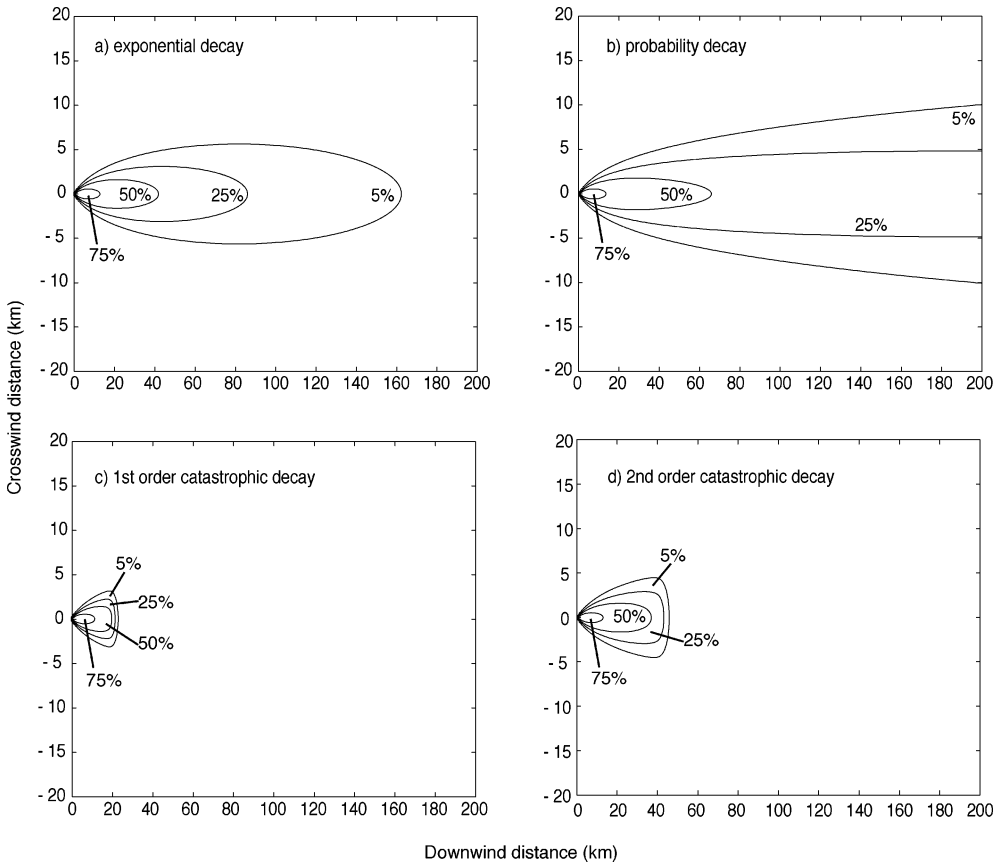

FIGURE 3. Cumulative death probability contours for the four decay models. The anthrax release scenario is described in the text. The decay rate constant for all models is 1.67 $\times$ 10^{-4} s^{-1}. The following constants were used: probability model ($V_f = 0.35$), first-order catastrophe model ($B = 0.1$, $C = 0.05$), and second-order catastrophe model ($B = 0.155$, $C = 0.05$).

outdoor, land and material surface type) could each result in distinct actual degradation curves and mathematical degradation constants. This adds to the complications and uncertainties regarding the effects of environmental degradation on appropriate decontamination response.

4. Discussion and Recommendations

There is a real need for better understanding and modeling of biological weapons agent viability degradation in different environments. Despite many studies of viability decay, understanding is fundamentally difficult due to the living nature of the agents. Viability decay depends on physiological factors in the agent and host that are impacted by agent growth conditions, the use of stabilizing materials in agent formulation, and host health. Many of these factors may be unknown at the time of a crisis. This emphasizes the vital need for immediate and accurate experimental sampling in potentially affected areas during crisis response. Sampling will provide actual, versus predicted, hazard. Predictive models, despite their deficiencies, are needed to efficiently provide information during a crisis (to direct sampling or other response functions). They are also needed for longer-term pre- and postcrisis planning. However, this work suggests that detailed maps of the hazard footprint, provided by current response models and research models that represent smaller-scale structures (e.g. urban street canyon models), are highly uncertain. This is at least in part due to the uncertainty in our knowledge and representation of agent environmental degradation.

This work underscores the need for three types of future research. First, better understanding and representation of viability decay in the environment can only come from detailed phenomenological microscale studies of microbiological system behavior, system responses to environmental stressors, and system repair mechanisms. Second, more work is needed to relate these basic science studies to parametrizations appropriate for response modeling. This will require more experimental data, particularly over longer time scales (from hours to months). Third, terrorism response models should provide probabilistic representations of hazard. These should be based on probabilistic representations of the uncertainties in the input parameters and model physical parametrizations, including agent environmental viability degradation.

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Supporting Information Available

A detailed description of the literature search. This material is available free of charge via the Internet at http://pubs.acs.org.

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