Smallpox Martyr Bio-Terrorism Scenario Modeling
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Abstract

This project is intended to model a martyr-type scenario in which a small terrorist group infiltrates a city after infecting themselves with a weaponized, vaccine-resistant strain of Variola major; agents of the group attack hospitals first, passing as flu sufferers until they become contagious. After panic begins to spread, as the population realizes that they would have to avoid medical facilities even if they become infected, the remaining faction infiltrates the city, spreading the virus further. With the mass panic and disease spreading, the city shuts down. Nobody is allowed in or out, effectively quarantining the city. Residents panic and remain at home in fear of infection, at which point the city stops functioning completely as infections spread and disease control units are helpless to intervene due to the quarantine and the population's general panic. After some time, control of the city is regained as quarantine is implemented, or a new vaccine to counter the modified strain of smallpox is developed, mass produced, and distributed en masse. After this point, the danger from the attack drops to zero as the remaining survivors have nothing else to fear from the now obsolete virus weapon.

1 Introduction

1.1 Actual Situation

If smallpox, or Variola, was released into a population, the result would be a global spread and the virus would cause hundreds of thousands or even millions of fatalities. The long incubation time of smallpox would make spreading the disease from one town to another or from one country to another extremely common. Smallpox cannot be aimed or targeted; once released, it will kill and infect indiscriminately. This means that the group releasing the disease would also harm their own families, friends, and allies. Despite these dangers, there are factions whose goal is only to cause panic at any cost, and once these groups have successfully obtained smallpox they pose a great threat to the rest of the world.

"Although declared stocks of smallpox virus exist only at the two World Health Organization repositories (the Centers for Dis- ease Control and Prevention [CDC] in Atlanta, Georgia, USA, and at the State Research Center of Virology and Biotechnology, also known as Vector, in Koltsovo, Russia), it is of concern that undeclared stocks may exist in military sites within the former Soviet Union, or that they were transferred from the Soviet program to programs in Iraq, Iran, North Korea, or elsewhere. The probability that such stocks exist is impossible to assess, but the catastrophic consequences of smallpox release in a biological attack cannot be discounted." (Jahrling, Huggins, Ibrahim, Lawler, and Martin 220)

1.2 Scenario

The scenario I am modeling is not considered in "Smallpox and its Eradication;" the conclusion of the passage involving a biowarfare attack using smallpox states that an attack would be unlikely (Fenner, Henderson, Arita, Je?ek, and Ladnyi 1344). However, this conclusion was made in the days after the eradication, before bioengineering was as easy and possible as it has become in recent years, and before terrorist groups, willing to sacrifice lives without strict regard for whose lives were being sacrificed, were known to hold any significant power in the modern stage. My scenario considers a vaccine-resistant strain and a well-planned, independent attack by a small group of terrorist extremists; the danger from this threat has greatly increased in recent years. According to Sderblom, this case is surprisingly likely and has the potential to kill millions of people or more around the world.

1.2.1 Chance of an Attack

"Intelligence agencies and international relations scholars are concerned that Russian researchers of the former Biopreparat, many whom are unemployed since the 1990s, and feel disenfranchised, could be tempted to smuggle and sell smallpox to those terrorist groups with the financial resources and microbiological expertise to use it, or further weaponize it. Marvin Cetron, president of Forecasting International Ltd, a risk assessment company working with both the US Defense Department and the FBI, has stated, "I think the chance is about eighty percent of terrorists obtaining smallpox..." Thereby, in the opinion of? experts, the potential for a serious smallpox attack is frighteningly feasible." (Sderblom 3)

1.2.2 Execution of Attack

"In this scenario, two "smallpox infected suicide terrorists" strategically target doctors' offices (in winter) to obtain a medical certificate to explain their absence from work. (They could even leave before seeing the physician). They blend in with people suffering flu symptoms in the waiting room, but they are already effectively spreading smallpox amongst staff and patients. A terrorist organization claims responsibility for the outbreak. Citizens are too terrified to seek medical attention, as they are now aware that medical facilities have been targeted. This is when the second stage of the bio-terror attack occurs. Smallpox is delivered to the target city through either aerosolized delivery, or through another infected set of suicide terrorists passing on smallpox through exhaled droplets. Mass terror is created by the paradox that smallpox needs to be contained and treated, yet the mass smallpox infection of patients and staff at hospitals causes citizens to stay away from medical facilities. A radio-talk-back host ponders on-air whether by attending the doctor to get checked for the flu, or vaccinated for smallpox, you may acquire... smallpox before the vaccination takes effect. Large segments of the community avoid medical treatment. The strain placed on the infrastructure of the city brings it to a halt: planes do not arrive or leave, police at roadblocks turn back fleeing residents, and the "terror" caused by the bio-terror attack is unmatched by any previously experienced health catastrophe. The economy is bought to a standstill and the bio-terrorists now have political influence as they have demonstrated their capacity to inflict terror. Worse still, a rumor circulates that the smallpox is a weaponized variant from the former USSR, for which there is no vaccine. Thus the

containment of infected people proves to be impossible even though WHO vaccines arrive quickly" (Sderblom 8-9).

1.2.3 Reaction to Attack

My simulation assumes that as the attacked population would panic, as Sderblum stated, and, as the city shut down, chaos would spread. The terror caused by the attack would remove many aspects of societal function, resulting in a near-primal state in which the region dissolves into an every-man-for-himself civilization. At this time, people would group together with others and avoid those who appear to be dangerous; with a fear of infectious diseases, those in the prodrome phase exhibiting flu symptoms would be avoided in most cases, but those showing a full body rash that the media has declared as dangerous would be avoided if possible. They will remain within the boundaries of the closed section of the world being simulated; it is assumed that if one person were to leave the region, another would enter at the same time from another, similar region, to fill the same place. All of the tendency numbers are relative and none of them are guarantees of movement in one direction or another; the influenced movement method in my model is a general case causing infected people to be avoided and causing healthy people to cluster in groups for safety or comfort.

1.2.4 Vaccine Resistant Smallpox

In my scenario, the agent used is a sample of the India-1 vaccine-resistant strain from the Vector Lab in Russia, at Novosibirsk, that was lost from the 20-ton vats that were being used to manufacture the biological agent. In a statement, the Russian scientists announced that they have lost some of their stock, and several countries now, other than the US and Russia, who are legally allowed to keep a sample at the CDC and Vector labs, are suspected to have strains either of India-1 or another sample of smallpox, including Iran, North Korea, and Iraq (Preston 95-99). If the strain used is not the India-1 strain, it may likely be a bioengineered virus, with the human IL-4 gene inserted into a smallpox strain, which could be created in as little as "four weeks," by using the book "Current Protocols in Molecular Biology," and would cost "about a thousand dollars for each strain. Virus engineering is cheaper than a used car, yet it may provide a nation with a weapon as intimidating as a nuclear bomb" (Preston 222, 225). A virus engineered with the IL-4 gene of the host species

provided two groups of mousepox-resistant mice with a 100 percent fatality rate. The pox-resistant mouse never stood a chance with only ten particles of the engineered virus in its blood (Preston 225-226). The accepted infectious dose of smallpox is between one and five particles, and the average person who is infected inhales much more than the minimum dose, so the test did not include unnatural numbers of infectious particles. "The main thing that stands between the human species and the creation of a supervirus is a sense of responsibility among individual biologists? It seems possible that someone could be playing with the genes of smallpox right now? No nation that wanted to have nuclear weapons had a problem finding physicists willing to make them" (Preston 228). Biologists that are willing to engineer a vaccine-resistant smallpox virus are likely in abundance as are physicists willing to create nuclear weapons. All it would take is one person with a purpose, or recruited to a cause, to create a biological weapon that would resist any immunization that the known world could supply.

1.3 Background

Smallpox, also known as Variola major, is a fast-spreading disease with a 100 percent susceptibility rate in humans who have not been immunized in the past 10 years. The only populations recently immunized are military personnel and emergency health control workers.

Smallpox has a fatality rate between 30 and 40 percent and spreads like wildfire both locally and globally, traveling around the world in a month because of the 2 week incubation period in which no symptoms are shown from the infected person, as they travel around, moving to uninfected cities or healthy sections of a population before the sudden outbreak catches them by surprise, creating many more victims for the disease. The disease then spreads in a similar manner to the first case in which an infected person travels to another city or another country. In today?s world of long commutes and frequent vacations and business trips, smallpox would travel around the world incredibly quickly, making quarantine almost impossible. Thus, the scenario created by the terrorist organization would spread to many major cities throughout the world, creating millions of cases and deaths. If the group of infiltration terrorists were to spend time in an airport, the result would be an almost global spread within a matter of weeks (Preston 232).

Also, the likelihood of the released strain of smallpox being either part of the vaccine resistant India-1 strain, as explained by Sderblom and Jahrling,

or a bioengineered virus, as explained by Preston, is quite high, which would negate the use of vaccine as a counter to the terrorist attack.
Because of the panic caused by the news that a weaponized, vaccine-resistant smallpox strain had been released, and the chaos resulting from the infiltration of the city and attack against health facilities, any city would quarantine itself. The panic would shut the city?s functions down, preventing any quarantine measures from being beneficial to the public. The method of attack would prevent the use of a military quarantine within the city, and the city?s self-quarantine would not be broken so long as infections run rampant and chaos reigns. (Sderblom 9)
(Fenner et al. 189)
If information were released to the public detailing the risk of infection at a hospital being much higher than that of at home, very few, if any, infected people would seek any medical treatment at all, which would then increase the likelihood of smallpox spreading to others in a city through face-to-face contact during transit or time spent in buildings, as the ventilation systems of many buildings, such as townhouses, apartments, and other large-scale city housing areas are susceptible to spreading smallpox over a large area, as was the case in the Meschede hospital in Germany in 1970, in which one victim infected 17 others, where only one of them had seen his face or been in a room with him (Preston 47; Fenner et al. 193).

2 Smallpox

2.1 Progression of Infection

In the beginning of an infection, the person does not realize he is infected with anything until 10-14 days after exposure, when prodromal symptoms begin, with the rash appearing two to four days later. The first symptoms could appear, however, as early as seven days after exposure, or as late as 17 days (Akhtar 23; Fenner et al. 5; "Medical Management of Biological Casualties Handbook" 62; Gober and Werth; "Smallpox," Utah Department of Health; "Smallpox Information Center"). This phase is part of what makes smallpox so devastating; during two weeks, infected people might travel to other places, and they then infect other people, making a quarantine nearly impossible ("Smallpox", World Health Organization [WHO]). The above graph shows a case study of several hundred people, exposed to smallpox, and examined the length of time from initial exposure to the beginning of prodrome symptoms. The mean of this data is 11.5 days, and

the standard deviation is 1.1 days. This will be modeled with the Python gauss(mu, sigma) function. This function generates a random number along a normal distribution given a mean, mu, and a standard distribution, sigma. Based on data from SE172.3. Downie; Mack. 1972: and WHO/SE/73.57, Litvinjenko et al., (Fenner et al. 188).

"The prodrome or preeruptive stage of the illness starts abruptly, with fever (usually 101-104F [38.3-40C)]), malaise, headache, muscle pain, prostration, and often nausea and vomiting and backache. The person usually appears quite ill. The prodrome usually lasts two to four days," with a mean of three days, and a standard deviation of about eight hours. "The person is not infectious until the end of the prodrome, when lesions develop in the mouth" (Akhtar, 27; Atkinson et al. 283; Gober and Weese; "Smallpox," Utah Department of Health).

However, when lesions develop, the rash has not yet begun, and diagnosis of a smallpox victim in the prodromal stage is difficult, as symptoms closely resemble those of flu sufferers. If someone suffering from smallpox is towards the end of the prodrome, placing him or her into a clinic or hospital with some flu victims has the highest infection rates of any realistic situation. The next day, when he or she is diagnosed because of the beginning of the rash, he or she may have already infected tens of flu patients unknowingly. These now infected flu victims will recover from the flu, and as the smallpox prodrome begins, they will likely be treated for relapse, perhaps in different hospitals or clinics, and the cycle continues.

After the prodrome ends, the characteristic centrifugal rash forms and the disease matures.

2.2 Advancement of Rash

day 1 of rash - macules and rash spread throughout body to concentrated areas on extremities (hands, feet, head) but covers entire body; macules begin to form papules

day 2-3 of rash - rash raises - papules progress slowly to form vesicles

day 3-4 of rash - fever returns in full force

day 3-5 of rash - vesicles begin to form pustules

day 6-12 of rash - vesicles have formed pustules, which are sharply raised, typically round, tense, and firm to the touch

day 13-20 of rash - pustules drain of fluid and form a crust - at this stage, infected people are no longer highly infectious, and the fever drops off as recovery begins - if a victim has survived so far, death is unlikely

day 21-28 of rash - crusts drop off, patient has recovered

(Medical Management of Biological Casualties Handbook 63; "Smallpox Disease Overview," CDC)

During the rash, all pustules and marks progress at the same speed; unlike chickenpox, in which an infected person may see pustules that are forming right next to a crust that is falling off. (Atkinson et al. 283-284)

This is an average progression of a case of ordinary smallpox; typically the victim will be fully healed between day 21 and 28 of the rash, as when the scabs drop off, the patient is no longer contagious ("Smallpox Information Center"). The values will be modeled with the mean of 24.5 and the standard deviation of 1.167 days of infection before the victim is cured and recovered because of the first and last days of the end of the infection being 21 days and 28 days, respectively, from the beginning of the rash.

2.3 Forms and Fatality Rates of Smallpox

There are five recognized forms of smallpox, where one of the forms is a severe case of another. These different variations of smallpox have different symptoms, vastly different fatality rates, different durations, and some slightly different infectious rates.

1. Ordinary-type smallpox exists in about 85 percent of cases (severity of infection is mostly random except that children and the elderly are more susceptible to a worse case, but the severity is mostly based on the intensity of the rash, and the severity of the prodrome varies in severity as well.) "In fatal cases, death occurred between the 10th and 16th days of the illness" (Fenner et al. 22; Hong), in the second week of illness due to toxemia ("Smallpox as a Bioterrorism Agent"), in "one to two weeks after infection as the bloodstream becomes overloaded with the virus" ("Dermatology", About.com). "Toxemia may be so severe as to cause death even before the rash is fully developed, but more commonly death, if it occurs, will be between the 11th and 15th day of the rash" ("Smallpox Information Center"). To model the fatality rate, the gauss function in python will be used with a mean of 13 and a standard deviation of 1 so that the third standard deviation corresponds with the minimum and maximum values of 10 days and 16 days. The fatality rate of ordinary-type smallpox is 25 percent.

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//commons.wikimedia.org/wiki/File *Hemorrhagic$_s$mallpox.jpg* (Akhtar 41-45; Atkinson, et al. 284-285; Center for Biosecurity, University of Pittsburgh Medical Center; Fenner et al. 4-5, 22, 32-34, 37).

2.4 Infectivity

2.4.1 Susceptibility

"The outbreak [of Variola] grows not in a straight line but in an exponential rise, expanding at a faster and faster rate. It begins as a flicker of something in the straw in a barn full of hay? but it quickly gives way to branching chains of explosive transmission of a lethal virus in a virgin population of nonimmune hosts. It is a biological chain reaction." (Preston 48). Unfortunately, historical data are available only from periods with substantial population immunity either from vaccination or from having survived natural infection. In the absence of natural disease and vaccination, the global population is significantly more susceptible (Center for Biosecurity, UPMC).

In the absence of immunity induced by vaccination, human beings appear to be universally susceptible to infection with the smallpox virus (Center for Biosecurity, UPMC). Inoculation has ceased for the public since the Eradication campaign ended in 1980. The vaccine only lasts with any potency for 3-5 years ("Vaccine Overview," CDC). Therefore, the public is, except for deployed military personnel and laboratory staff engaged in work with vaccinia and related viruses, 100 percent at risk for infection with smallpox. In a city such as the model simulates, fewer of these people would be present than could be simulated with any degree of equal representation: much fewer than 1 in 5000 people in the U.S. are either deployed military (as deployed personnel would not be in the United States) or high level staff at CDC, the United States Army Medical Research Institute of Infectious Diseases [USAMRIID], or other similar laboratories, and the risk of a vaccine-resistant virus being introduced is high, so people with immunities are excluded from the model.

2.4.2 Rate of Infectivity over Time of Infection

"The maximum infectivity of cases of smallpox was during the 1st week of rash, corresponding to the period when the lesions ? had ulcerated and were releasing virus into the secretions of the mouth and pharynx? At this stage the skin lesions were intact: the large amounts of virus later shed

from the skin were not highly infectious because of the physical state of the virus particles, enclosed within hard dry scabs. For example, Mack (1972) found that the vast majority of cases infected after contact with cases of smallpox that had arrived in Europe from endemic countries while incubating the disease occurred within 3 weeks of the initial time of exposure?.in rural Pakistan Mack et al.. (1972b) found no evidence of significant transmission during the prodromal period. Theoretically, cases remained infectious until the last scab had separated (usually from the soles of the feet) but the level of infectivity fell off greatly as the lesions? healed during the latter part of the 2nd week of the disease" (Fenner et al. 189).

Persons carrying the virus during the incubation period cannot infect others. The frequency of infection is highest after face-to-face contact with a patient after fever has begun and during the first week of rash, when the virus is released via the respiratory tract. Although patients remain infectious until the last scabs fall off, the large amounts of virus shed from the skin are not highly infectious. Exposure to patients in the late stages of the disease is much less likely to produce infection in susceptible contacts (Center for Biosecurity, UPMC).

"Smallpox may be contagious during the prodrome phase, but is most infectious during the first 7 to 10 days following rash onset" ("Smallpox Disease Overview," CDC).

"The virus is readily found on the skin, in the oropharynx, and in the reticuloendothelial system throughout the rash phase (a highly infectious period from the appearance of enanthema until day 10 of the rash)" (Gober and Weese).

"The patient was most infectious from onset of rash through the first 7 to 10 days of rash. As scabs formed, infectivity waned rapidly" (Smallpox Information Center).

The infectious period of smallpox is "From the time the rash appears - particularly in the first week of illness - until the scabs fall off" (Akhtar 20).

"At the late stages, infection becomes a much less serious risk. So in short, there are roughly 8-9 days of serious infection possibility with smallpox, 3-4 days in which infection is a low probability, and approximately 12 days in which smallpox infection is no threat to others" (Feasel).

In summary, Most infections take place during the last day or two of the prodrome and the first ten days of the onset of the smallpox rash, with the exception of confluent smallpox, in which the infection rate does not significantly drop off after the first ten days, but only after about 20 days when the scabs form and cover the sores. In all other forms of smallpox, the peak infection rates occur around seven days after the beginning of the

rash, and drop quickly after day ten or 11, reaching lower values around day 12 or 13 and continuing to drop until around day 20; when the scabs form, the infectivity of a victim is very low. persons with a severe rash [hemorrhagic or malignant or confluent] and involvement of the mouth and pharynx are more infectious than those with a slight rash (Akhtar 96). Infection for smallpox during the prodrome begins at a very low value for the first two days, then rising quickly during the second, third, and fourth days. In the case of hemorrhagic smallpox, with a prodrome of double the length of the other forms of smallpox, infectivity remained constant after the third day, when the rash would likely have began on the inside of the throat of the victim, and remained at that constant until the rash began. Because of the lack of available data to accurately graph this data, I created my own quartic function model for the infectivity of a victim over time for confluent smallpox and nonconfluent smallpox. My equation for nonconfluent smallpox peaks around t=7 days, drops off at a somewhat steep rate after day t=10, and is concave down for the remainder of the days until t=20, at which point the simulation assumes a much lower rate, as at this time the patient is usually completely scabbed over. For hemorrhagic and malignant smallpox, the equation was multiplied by 1.1 to show the slightly increased infectivity of the disease in those two cases. The equation is: -5.715*10-5*t4+0.002557t3-0.0383t2+0.181t+1 My equation for confluent smallpox also peaks around t=7 days, but does not drop off at the same rate after day t=7 because of the continued high infection rate; instead, it maintains a gradual decline and reaches a similar low point around t=20. The equation is: -2.3564*10-5*t4+0.00163t3-0.0346t2+0.181t+1.015

2.4.3 R-zero, the Rate of Infectivity per Infected Person

In the past, patients suffering from Variola major (the more severe form of the disease) became bedridden early (in the phase before the eruption of rash) and remained so throughout the illness. Therefore, the spread of infection was limited to close contacts within a small vicinity. However, the estimated R-zero value, or the number of people infected from one case, has been estimated to be between three and 20, where an R-zero of five or more would spread "explosively," which would "get the world to millions of smallpox cases in a few months? It has taken the world twenty years to reach roughly fifty million cases of AIDS. Vari-

ola could reach that point in ten or twenty weeks" (Preston 47-48). Some experts have estimated today's rate of transmission to be more on the order of 10 new infections per infected person (Center for Biosecurity, UPMC). "The other five experts disagreed with one another, sometimes sharply, but in general they found that smallpox would spread widely and rapidly. They argued forcefully with each other (as scientists do), but in the end? ?Our general conclusion was that smallpox is a devastating biological weapon in an unimmunized human population," one of the participants said. ?If you look at the real-world data from a 1972 outbreak in Yugoslavia, you find that the multiplier of the virus was ten: the first infected people gave it to ten more people, on average. Basically, if you don?t catch the first guy with smallpox before he kisses his wife, it goes out of control. We could be dealing with hundreds of thousands of deaths. It will absolutely shut down international trade, and it will make 9/11 look like a cakewalk. Smallpox can bring the world to its knees?" (Preston 213).

In summary, According to Preston?s experts and the UPMC Center for Biosecurity, if the first person with smallpox is not quarantined before he infects another, there will be no method of stopping it from continuing to spread. If the first person or people do not want to be quarantined or stopped, as in a bioterrorist attack, the disease will spread globally, killing hundreds of thousands of people. After each two weeks, the number of people infected increases in a degree of magnitude: 10 to 100 to 1000 in the span of a month. The rate of R-zero was 10 in an era of mass vaccinations; with a population with a 100 percent susceptibility rate, R-zero will likely be higher; this will not be shown in the model. The R-zero of the model will remain at 10, and the number of others infected beyond R-zero=10 will travel, as Preston explains on page 232, to many places, and they will spread the infection to other cities, states, provinces, countries, and continents. The simulated infection rate will be 9¡R-zero¡11 to account for differences in exact populations and situations, but it will be focused around an R-zero of 10, as the predictions show.

2.5 Transmission

2.5.1 Inhalation

Smallpox virions behave like smoke particles, and are almost exactly the same size (Preston 47). To put this into perspective, if one were in a room in a hospital where there was a fire in a room in the same building, anyone who could smell smoke, would likely be infected if there was

a smallpox patient instead of a fire in the same room. The infectious dose of smallpox is between one and five virions, making the disease incredibly dispersible, as it does not need to be concentrated in order to infect (Preston 45). "Two hospital outbreaks in the Federal Republic of Germany, at Monschau (Anders Posch, 1962) and Meschede (Wehrle et al., 1970), seem certainly to have been airborne. In the Meschede outbreak an electrician who had just flown back to the Federal Republic of Germany from Karachi, Pakistan, and who, it transpired, had never been successfully vaccinated, was admitted 10 days later to the isolation ward of a large general hospital with a feverish illness that was suspected to be typhoid fever. He was confined to his room, and 3 days after admission developed a rash. Smallpox was confirmed by electron microscopy 2 days later and the patient was then transferred to the smallpox hospital. In spite of rigorous isolation of the patient (because of the suspicion of typhoid fever) and, after smallpox was suspected, the vaccination of all patients and nurses in the general hospital (in several cases with inactivated vaccine), or inoculation with vaccinia-immune globulin, 19 further cases of smallpox occurred there, on all three floors of the building in which the index case had been nursed. The dates of onset of these cases are shown in Fig. 4.9A. Seventeen cases occurred within one incubation period, counting from the 3 days during which the index case was in the hospital and infectious; the last 2 were room contacts of earlier cases as indicated. The locations of these patients within the hospital are given in Fig. 4.9B, which also shows the results of tests on the carriage of smoke through the hospital." (Fenner et al. 192) In the Meschede case, a smoke machine was used to recreate the possible spread of smallpox particles. This is the Fig. 4.9 described in the above passage. (Fenner et al. 193) Smallpox is transmitted mainly from person to person by infected aerosols and air droplets spread in face-to-face contact with an infected person after fever has begun, especially if symptoms include coughing, but infection can and definitely did occur in over 15 cases from one isolated source without any face to face contact at all, over three floors of a building, and one case in which the infected person was visiting for no more than 15 minutes in a hallway adjacent to the hallway containing the closed room of the infected, which justifies an increased spread of the possible infection in the model.

2.5.2 Contact Transmission

The disease can also be transmitted by contaminated clothes and bed-

ding, though the risk of infection from this source is much lower. Naturally, smallpox would be more infectious from direct contact with a victim, but inhalation of smallpox virions is the most common method of transmission (Center for Biosecurity, UPMC). Fenner discusses the transmission of smallpox through scabs on clothing or bed sheets: "the most important finding was that, in Madras, virus on such objects was rapidly inactivated, even when they were heavily contaminated; he concluded that fomites, or particles of smallpox-infected biological material, were of little importance in the transmission of smallpox in India. In temperate climates virus in scabs could survive on fomites such as cotton for long periods of time (MacCallum McDonald, 1957) ; however, virus in scabs rarely appears to have been a source of infection" (Fenner et al. 194). Virus transmission via infected clothing is a very minor risk, and contact will not be included in the simulation other than a higher risk of infection based on proximity.

2.5.3 Animal Transmission

There is no animal reservoir. Insects play no role in transmission (Center for Biosecurity, UPMC).

Therefore, the vast majority of smallpox infections were caused by inhalation of particles transmitted from oral cavities through coughing of those infected; thus, it stands to reason that infection rates would be higher upon closer proximity or upon more time spent near an infected person. In my model, the rate of infection will be a cubic function: each unit that a healthy person moves towards one who is infected while inside the infection range will increase the likelihood of infection threefold.

2.6 Complications After Recovery

Between 65 and 80 percent of people who recover from smallpox will have some form of pockmarks on their faces. In 0.9 percent of survival cases, blindness occurs, typically in those recovering from confluent forms of smallpox (confluent, flat, hemorrhagic). In 1.7 percent of cases, arthritis is found (Fenner et al. 47, 50). In 1-4 percent of recovered cases, "blindness from corneal scarring, growth abnormalities in children, and disfiguring or even physically debilitating dermal scarring" occur (Medical Management of Biological Casualties Handbook 64). "Blindness from scars on the eye is common" (Hong). These data sets fit well together; 0.9 percent of cases result in blindness, which reduces the simulated person?s vision to zero, 1.7 percent of cases cause debilitating

dermal scarring or arthritis, which reduces the simulated person?s movement by 80 percent, and the remaining percent receive disfigurations or growth abnormalities in the long term which do not affect the short-term model.

3 Research, Modeling, and Simulation

3.1 Objectives

The purpose of the project is to use a sugarscape based modeling system in Python in order to determine the actual death toll caused by a scenario that relates to the one described above. In my model of the scenario, the modeled population is small, but the representation of 5000 in a small township or city block is representative of the entire city. The representation is used because of the limitation in computing power; while it would be useful to visualize the social network of the entire city, processing power limits prevent a larger world from being simulated over the same period of time, and the visualization of an entire city?s social network is in no way necessary. The same situation would take place in every section of the same city and every infected city in the world, so the result will likely be universal; the long incubation period coupled with a few attacks in key cities or airports would guarantee a similar case taking place around the globe in many if not all major cities. The model is not a physical representation of the population, but rather a visualization of the interactions between the 5000 people in the model as time goes on. Different people in the model belong to several different social groups, as in the world today. If one person from one group infects another person, the newly infected person would infect another group of people from a separate location or association; this is the way in which a contagious disease spreads rapidly in a large city. The purpose of the simulation is to show the probable outcome of a situation with regards to the time that the situation is brought under control; that is, when a successful quarantine has taken place or when a new vaccine has been developed and distributed to those not already infected. It is assumed that once the quarantine or vaccine has been implemented that no more infections will take place in the area. The statistics for infections, recoveries (people who have become immune naturally), and deaths will then freeze as the epidemic ends, except for the continued progression of the disease in those already infected.

3.2 Related Work

Much research has been done in the field of epidemiology with regards to smallpox, focusing on the containment of an outbreak. Several government programs have made advances on simulating a smallpox outbreak from an accidental beginning, but no projects that extended periods of research have uncovered have dealt with a planned suicidal bioterrorism attack using knowing human agents to spread the disease. No model has been found that gives percentages of any statistics by time after the beginning of the infection.

3.3 Rationale

This research will specify a disease - smallpox, or the Variola virus - and attempt to determine the fatality rate by percent in the large city in which the attack and infection first takes place over time. It is assumed that similar scenarios will take place in other cities globally, but with slightly reduced fatality rates on average, as some other locations will likely be able to prevent the outbreak. The project makes the assumption that vaccination and containment are ineffective in the scenario for the duration of the simulation, due to the vaccine-resistant strain or bioengineered strain released and the panic of the general population; the scenario described in the introduction is taking place. The model has been created to estimate the fatality rates based on the response time with regard to ending the panic of the city and creating a new vaccine that is effective against the India-1 strain or the bioengineered strain.

3.4 Procedure and Methodology

Python will be used in the final project where NetLogo, an agent-based modeling program, in which a pre-written program modeling a generic virus infection on a population was used to obtain a basic understanding of the intended result of the project. This is a screenshot from the NetLogo program; red agents are infected, green agents are not, and gray agents are immune.
The Python model will be an agent-based model with circles representing the people in the area; each point can either be occupied by one agent or empty. In an agent-based model, agents, or visual representations, are used to simulate real people or things. The model is not an exactly physical model, but rather a social one; instead of showing where an person is in the city at a given time, it shows who or how many other people the first

person is near; two agents close together implies that two people would spend time in close proximity to one another, or in a situation in which one person would likely infect the other. If several agents are all very close, the model may be representing a party or social event in which the people are all in contact with one another. The model also does not represent a definite proximity, but rather an average proximity of the people in that area over the four hour period being modeled by one step of the program.

Also, many researched works on smallpox exist, containing many case studies, but none that could be found detail the average time of death after the first symptoms; several individual points and generalizations have been found. In cases such as these, the Python gauss(mu, sigma) function will be used as a model from these generalizations. The mean will be the middle of the data range and the third standard deviation on either end will be equal to the minimum and maximum values.

Testing will be done with regard to statistics for previous outbreaks of smallpox and recorded death rates with regard to variables in these outbreaks. Infection rates will also be used; infectivity has been increased or decreased as a whole until an R-zero value of 10, with a margin of error of no more than 1, is reached.

An assumption made is that people need to sleep and do not, therefore, move constantly: on average, a person would be stationary for 8-12 hours during the day, shown by the representation being motionless for two to three steps every six-step day, either sleeping or in a more sedentary activity. In the code, there is a random element included in the movement, showing that some people are less inclined to movement and more inclined to sleeping for a longer period of time than others.

With many sores on the feet of a smallpox sufferer, coupled with the symptoms and illness of the disease itself, someone infected with smallpox would likely move much slower than one who is not infected (Akhtar 72). This is modeled by showing that those infected with smallpox are only 50 percent as likely to move around as a healthy person, and that those with flu symptoms but no rash, in the prodrome of smallpox, with a malaise accompanied with other unpleasant symptoms, are only 60 percent as likely to move around, simulating decreased towards mobility.

3.4.1 Methods, Techniques, and Construction of Program

- Create a set of data points to track the number of agents in the world which are healthy,

carrying the disease, in the prodrome of smallpox, infected while exhibiting a rash, recovered and therefore immune, and dead.

- Define the number of agents in the world (5000).
- Define the number of terrorist representations in the world (10).
- Create the agent class:
  - Constructor of agent: (self, canvas, x, y, health)
  - Self is required for a constructor in Python
  - Canvas describes the window in which the agent exists
  - X and Y are the coordinates in the world
  - Health describes the status of the agent at the beginning of the world; either the agent will be healthy or the agent will have been infected as one of the ten terrorists in the model
  - Create variables that affect the agent?s movement:
  - The agent can see randomly 3, 4, or 5 spaces away determined at startup (if the agent sees another agent, the movement of that agent will be influenced accordingly. The numbers were chosen in relation to the maximum range of infection, 4 spaces. Some people have greater situational awareness than others and will be able to detect a possible threat before it becomes an actual threat, while others can detect a threat as it becomes a threat, and still others are unaware until long after the threat has passed.
  - The agent will have a tendency to move with a random element accounting for 30 percent of the tendency; outside of this value there are many instances in which the agent will not move; however, this value accounts for the fact that some people are more inclined to movement than others.
  - Agents are given values for coordinates on the world and Boolean values for whether or not they are immune; at the beginning of the program, no agent is

immune.

- At this stage in the development, agents who are infected will determine the duration of the stage of infection in which they are in at the moment.
- The disease information array is created, with 6 pieces of information:
    1. the stage of the infection in which the agent is currently in (carrier, prodrome, infected, healthy)
    2. the type of smallpox that the agent is infected with, with an empty string (??) if the agent is not infected (ordinary, confluent, modified, malignant, hemorrhagic)
    3. the status of the infection with regards to appearance: if the agent appears sick (is either in the prodrome phase or exhibiting a rash), the value of the Boolean is True
    4. the time (in days) since the beginning of the stage of infection the agent is currently in
    5. the time (in days) at which the agent will progress to the next stage of the disease or recover
    6. the time (in days) at which the agent will die from smallpox (if the agent will recover, the value is set at 100)
    - The agent is given a method which is used for debugging purposes, which shows the values of all of the aforementioned data.

- Create the method in which if the agent is exhibiting symptoms of infection, whether in the prodrome or rash phases, the infection of other agents takes place.
    - During the agent?s move, a similar method to the vision method is used; every space within 4 (the infected range) spaces is added to a list, all empty spaces are discarded from the list, and all remaining agents are processed.
    - Before the agents can be processed, however, the state of the current agent must be evaluated to determine the potential

risk factors for the other agents. Depending on the length of time that the agent has been infected, the potential risk can be very high or very low.

- If the infected agent is in the prodrome phase, the risk of infection is low; this corresponds to the low chance of infection resulting from a person who has not shown signs of the rash of smallpox. However, as the agent endures the prodrome for longer and longer periods of time, the risk for infection rises to show that the infected person develops patches on the back of the throat in which smallpox virions can escape the body.
- If the infected agent is exhibiting signs of the smallpox rash, the value differs greatly. An agent with ordinary or confluent smallpox has a multiplier of 1.0, where an agent with hemorrhagic or malignant smallpox has a multiplier of 1.1, accounting for the increased infection caused by greater numbers of smallpox virions in the bloodstream of the infected person. Agents with modified smallpox have a modifier of 0.2 to account for the low risk of the disease; it is by far the most mild of the forms of Variola.
- After the multiplier is calculated, the duration of the rash is factored in: the equations shown in the bottom of the "Rate of Infectivity over Time of Infection" section on page 10 are used to determine the complete risk factor of the infection taking place.
- For each agent within the infection range, a random number is compared to 3 to the power of the distance between the two agents * the aforementioned risk factor * a common multiple that scales the random number to a suitable amount; this value plays a key role in the R-zero value, and the common multiple was the key element that was changed to obtain an R-zero of 10.
- A much lower multiple is used to determine the risk of infection for those who are already immune and

have recovered from the disease once.

  - If the random value is higher than the multiplied factor, the agent is not infected, and is discounted from the remainder of the first agent?s actions during that time step.
  - However, if the random value is lower, the agent will become infected. The agent takes on one of the forms of smallpox, with a probability of taking each form depending on the percentage of cases of each form obtained through research. The newly infected unit then becomes a carrier of smallpox, and the time until the agent progresses to the prodrome phase is set.

- Create the method in which the agent progresses one sixth of a day with regards to the smallpox infection:
  - Increase the value of disease (the array of infection data) which tracks the time since the beginning of the stage of infection by one sixth of a day
  - Check if that value is greater than the value determining when or if the agent will die; if it is, set the value in disease that controls the stage of the infection to ?dead,? which removes the agent from the simulation
  - If that is not the case, check if the value is greater than the value determining when the agent will progress to the next phase of the disease; if so, check which part of the disease the agent is currently in.
  - If the agent is merely carrying the infection without symptoms, change the first value in the disease array to ?prodrome,? the Boolean describing visibility of infection to True, the length of time since the beginning of the stage of infection to 0, and the time at which the agent will progress again to a random value (rounded to the nearest sixth) as detailed in the description of the form of smallpox above. If the agent is infected with hemorrhagic type smallpox, there is a large chance of fatality during the prodrome, and this is represented with a potential

change in the final value of disease, in which the time until death is recorded.

  - If the agent is in the prodromal phase, the disease array becomes [?infected?, stage of disease, True, 0, a random aspect determined by when the agent will recover as detailed above in the description of the progression of an infection of smallpox, and another random value showing when or if the agent will die (again rounded to the nearest sixth]

  - If the agent is already infected and has survived until this point, it recovers, setting disease to [?healthy?, ??, False, 0, 0, 0], showing that the agent will no longer progress in the disease and will not die. The agent will become immune, and the corresponding Boolean will change to show this. The potential long-term effects of infection will be calculated, with a 0.9 percent chance of blindness, which reduces the vision of the agent to zero, and a 1.7 percent chance of developing severe arthritis, which cuts the mobility or tendency of the agent to move in half.

- Create the method in which the agent progresses one sixth of a day with regards to the location of the agent in the simulated world:

  - The agent views each location which it can see (as defined by the vision variable, where one step is either one location immediately to the left, right, top, or bottom) and stores it in an array

  - The array is pruned, weeding out any values that do not contain an agent (as only agents affect the movement of other agents)

  - A coordinate of influenced movement is created; it will be affected by all agents that can be seen

  - Iteration over every agent in the array of visible agents considers the disease of the viewed agent (a more severe form of the disease has a greater influence on the agent viewing it), the proximity of the agent (an infected agent immediately next to the

agent viewing it will cause a greater response than one far away), and the possibility that the other agent may be friendly (agents, like people, tend to gather in groups for comfort). At this time, people would group together with others and avoid those who appear to be dangerous; with a fear of infectious diseases, those in the prodrome phase exhibiting flu symptoms would be avoided in most cases, but those showing a full body rash that the media has declared as dangerous would be avoided if possible.

– To account for human error and ignorance, the tendency to avoid a victim in the prodromal stage will add 0.4 to the influenced coordinate in the direction opposite the infected agent, the tendency to avoid a victim suffering from smallpox with the ordinary or modified rash will add 0.6 to the influenced coordinate, and the tendency to avoid a victim with a confluent, flat, or hemorrhagic rash, because of the appearance of the infected, would be greater: 0.9. Those already infected will not care for the appearances of others as much, as they will have already resigned to their fate. Those in the prodrome phase will avoid others who are apparently sick by adding 0.2 to the influenced coordinate, while those with the rash will not make any attempt to avoid others who are infected at all. They will try to avoid those who are not apparently infected, however, for fear of being shunned or rejected or infecting others. They will have the same tendencies to avoid the healthy people as the healthy people have of avoiding them. All of these numbers affect the influenced coordinate, but are not guarantees of the movement itself.

– The movement is calculated from the influenced coordinate by adding a value to a list for each space between the actual coordinate and the influenced coordinate in each direction, adding a ran-

dom number between 0 and 3 of cases in which the agent would not move to the same list to represent sleep or a briefly stationary agent, and then taking a random value from that list as the final coordinate.

- There is a random aspect to the movement: the movement tendency described in the creation of the agent is the chance that the agent will move if healthy.
- After this value is calculated, infected and prodromal agents will be less likely to move because of the malaise and other symptoms caused by the prodrome, and the more severe symptoms during the rash stage of the infection: agents in the prodrome will move 60 percent of the time and agents exhibiting the rash will move 50 percent of the time they normally would after the calculations above were made.
- If the agent is healthy or only a carrier of the disease without showing any symptoms, it then progresses as the method above describes.

- After the creation of the agent class is completed, the basic world is formed. It is a Sugarscape model, displaying a closed, square, 200X200 world of locations.

- During each time step (representing one sixth of a day), each agent moves, possibly infecting others and progressing through the disease.

- For debugging purposes, if an agent?s visual representation is clicked, the agent will display information about itself, including its location, disease status, and personal status involving mobility and vision.

- At the creation of the world, 10 terrorist agents, already in the carrier stage of the infection, are inserted into random locations, followed by 4990 healthy agents.

- After each time step, the world is redrawn. Agents that have moved are now shown in different locations, and agents that have progressed in the disease or become infected are now different colors.
  - Green agents are healthy.

  - Yellow agents are infected with smallpox but have not begun to show symptoms.
  - Orange agents are currently in the prodromal phase of the infection.
  - Red agents are exhibiting a fully formed smallpox rash.
  - Blue agents have recovered and are now immune.

- Along with the world visualization, a running histogram is also created. The histogram shows the number of agents in each of the above categories as well as the total number of living agents (white) and the total number of dead agents (gray). It updates every step to show the 800 most recent steps.
-
-

The histogram described above shows a time span of about four and a half months.

2

3.5 Expected Results and Value to Others

This project can be expected to provide an understanding of the fatalities and infection rates of such a population in a major city in a scenario as described in the abstract, depending on when the situation falls back under control and a vaccine is created. The chance of this type of scenario being a possibility ranges from predictions of 60 percent to 80 percent, infection rates slightly after 2 months are around 50 percent of the population of the city, and about 75 percent of the population of the city targeted after about 3 months are expected to be infected.
The simulation will show the expansion of the infection over time as well as the expected result of the spread of the disease at different times. My simulation will show the statistics of the population during an attack based on time after the beginning of the attack. Depending on how quickly control can be regained and how effective the quarantine effort is; different percentages of the population in the city (as shown by my model) could be saved.

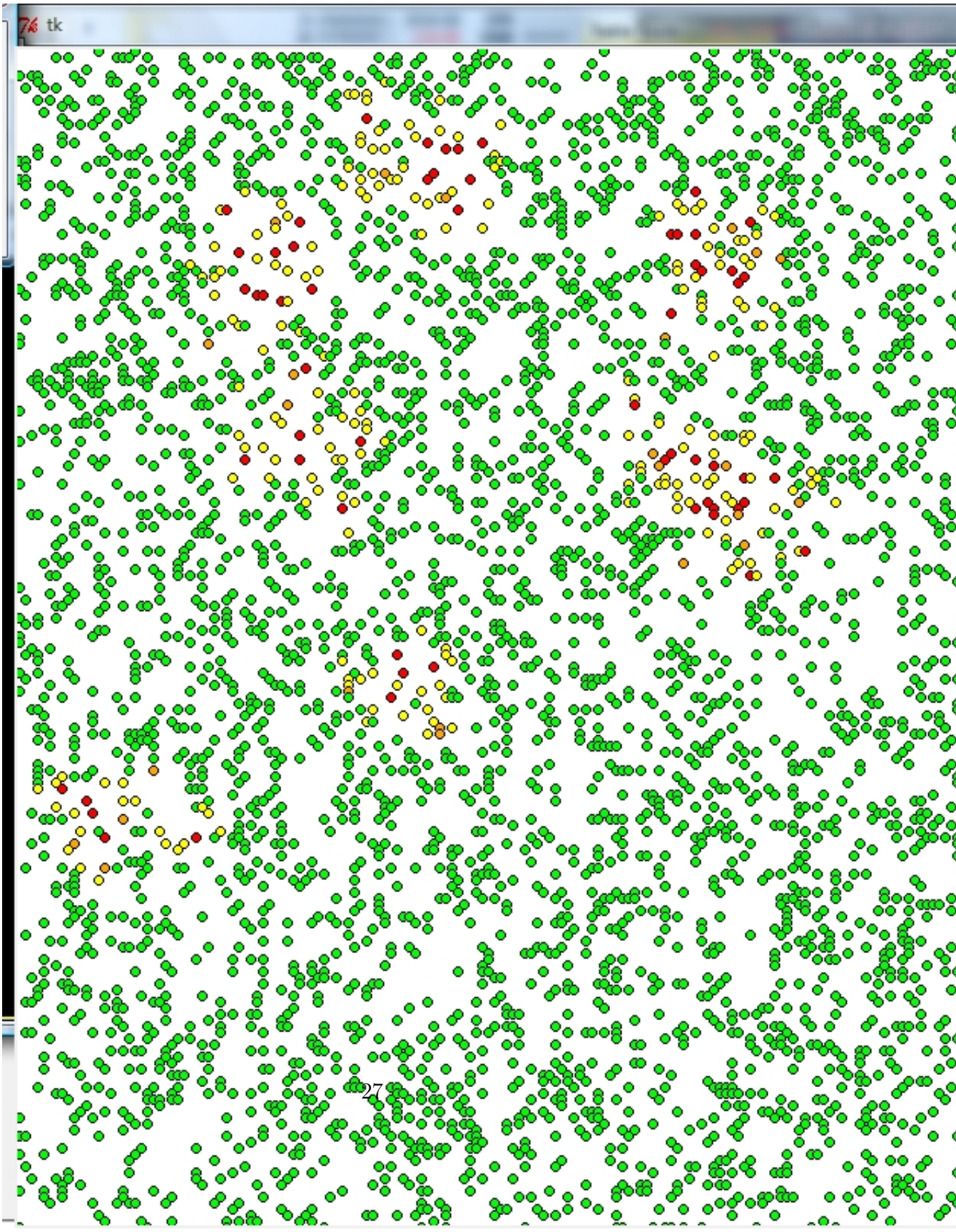
Trial	Healthy	Carriers	Prodrome	Infected	
1	4709	217	33	39	
2	4732	189	24	53	
3	4716	202	28	51	
4	4650	252	34	62	
5	4721	189	45	44	
6	4694	205	39	60	
7	4710	211	22	56	
8	4713	197	30	58	
9	4678	218	34	67	
10	4724	188	39	47	
Average	4704.7	206.8	32.8	53.7	

4 Conclusions

4.1 Data

The data from the trial runs are accompanied with a screenshot of the program at a point in time close to that shown in the data tables. After 10 trial runs with 10 terrorists in the scenario, the end results were as follows: Out of 5000 people in the modeled location:

1. After 1 month (180 steps = 30 days):
2. After 2 months (360 steps = 60 days):
3. After 3 months (540 steps = 90 days):
4. After 4 months (720 steps = 120 days):
5. After 5 months (900 steps = 150 days):
6. After 6 months (1080 steps = 180 days):
7. After 7 months (1260 steps = 210 days):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4.2 Summary

The above graph shows, by percent, the relationships between the numbers of healthy agents, agents carrying smallpox, agents in the prodrome of smallpox, agents exhibiting a rash, agents who have recovered, and agents who have died over the seven month time span of the program. It is assumed that with the graph as a representation of the population of the city, at the point in which control is regained, the quarantine will be effective and the vaccine will be given universally, stopping the spread of the disease. Therefore, given the data above, if control is taken and a vaccine is developed one month exactly after the attack begins, the city will have had 6 percent of its population infected, and most likely, around 2 percent of the population would die by the end of the outbreak. However, if control is not taken and a vaccine is not developed for four months, 94 percent of the population would have been infected and between 30 and 35 percent of the population would die.

2

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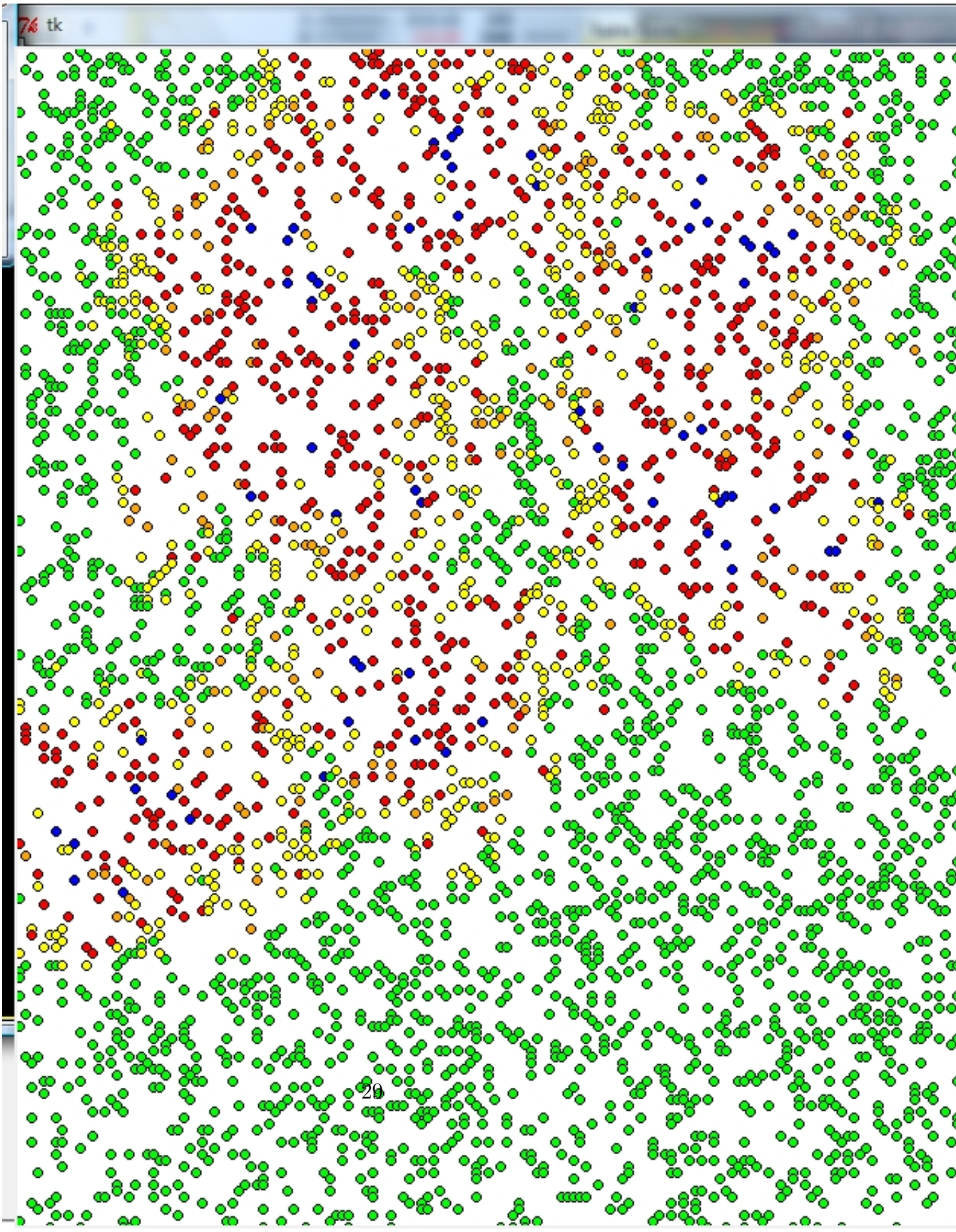
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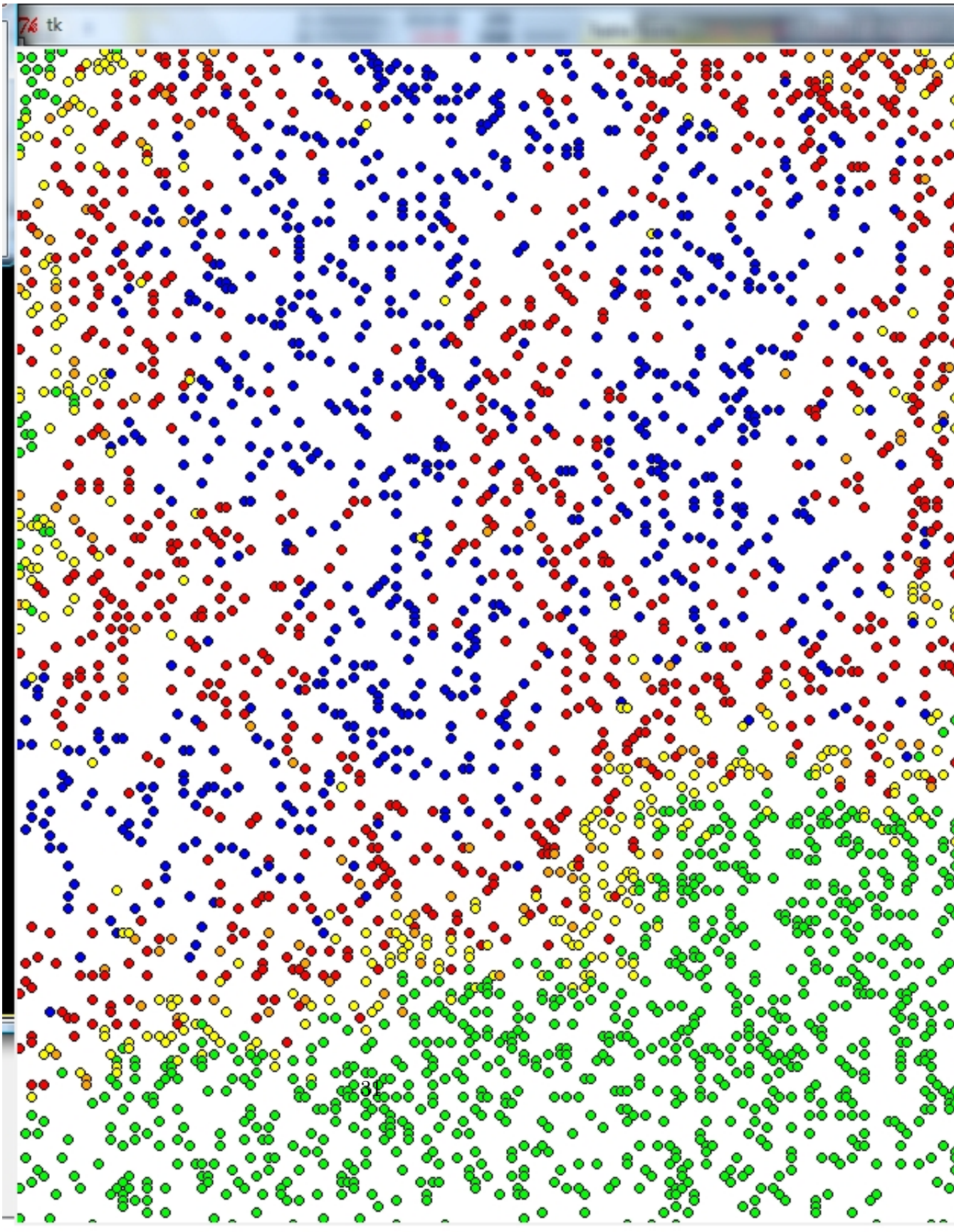
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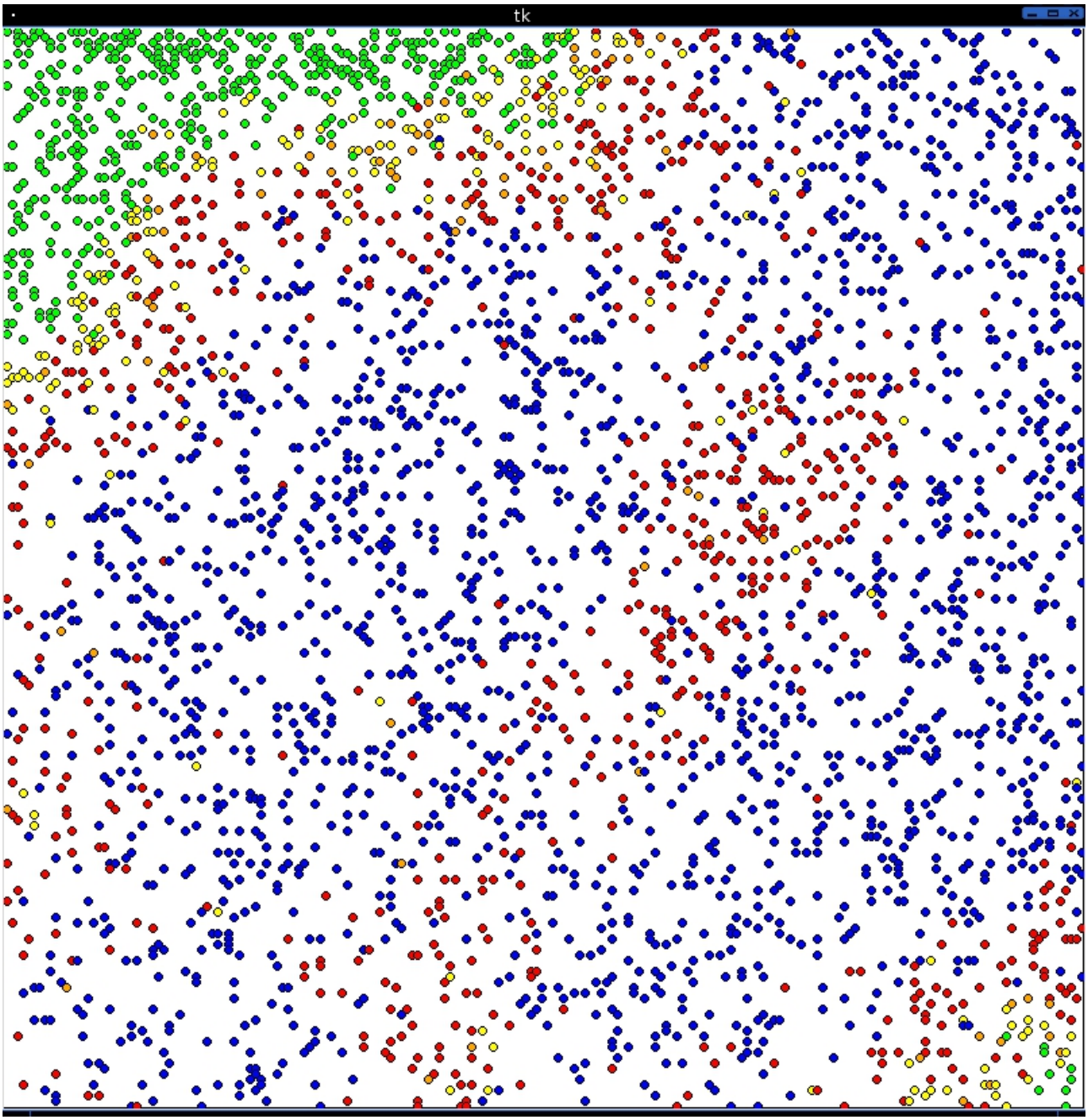

Trial	Healthy	Carriers	Prodrome	Infected	
1	39	69	29	403	
2	69	91	44	573	
3	3	20	11	241	
4	101	57	25	282	
5	0	2	4	206	
6	2	1	4	109	
7	302	127	40	387	
8	63	51	27	223	
9	0	4	6	257	
10	36	38	26	213	
Average	61.5	46	21.6	289.4	

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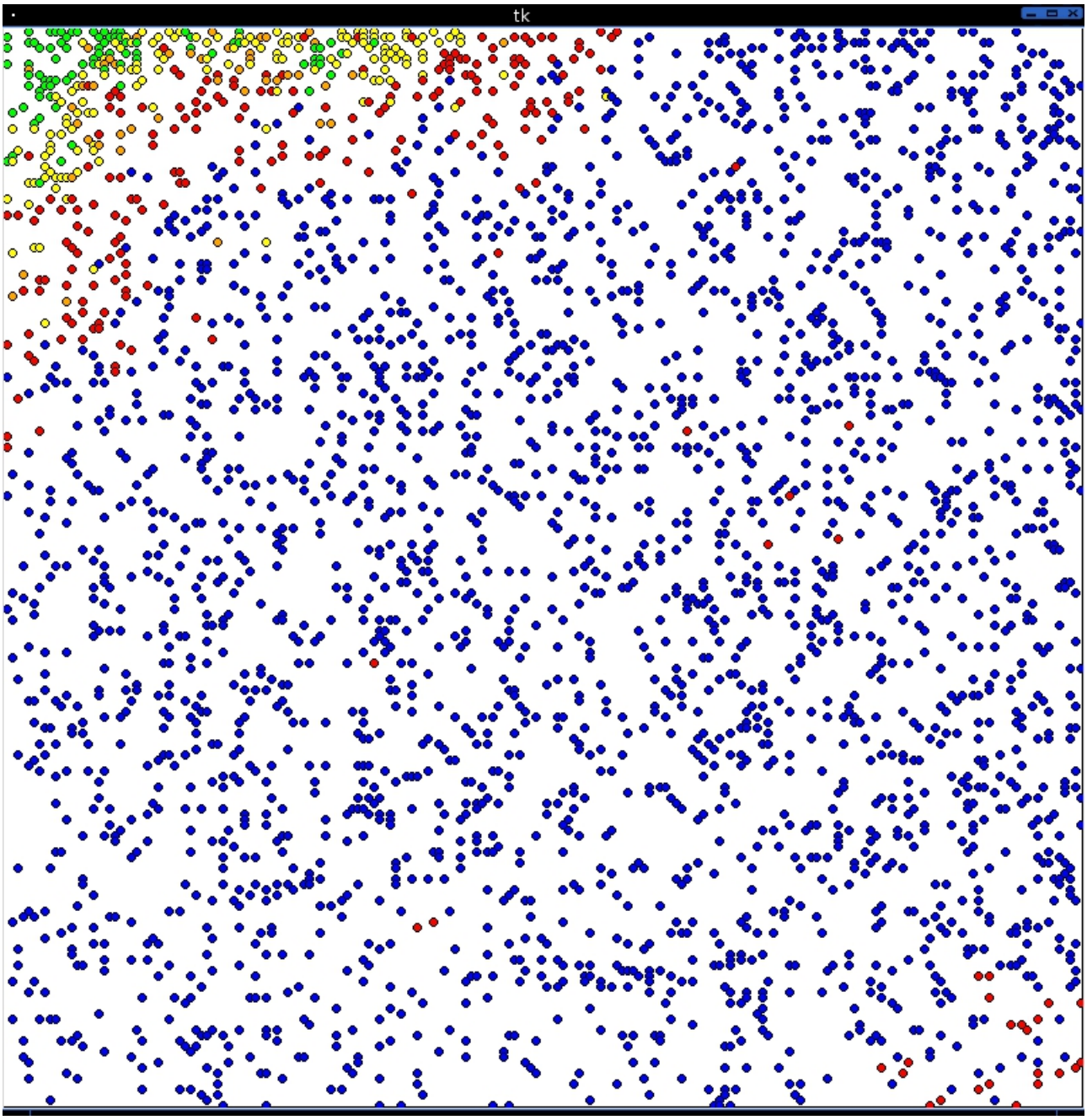
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Trial	Healthy	Carriers	Prodrome	Infected	
1	2	11	8	59	
2	4	16	7	83	
3	0	0	0	15	
4	3	20	13	85	
5	0	0	0	4	
6	2	0	0	1	
7	19	100	38	196	
8	5	15	6	61	
9	0	0	0	3	
10	1	3	2	48	
Average	3.6	16.5	7.4	55.5	

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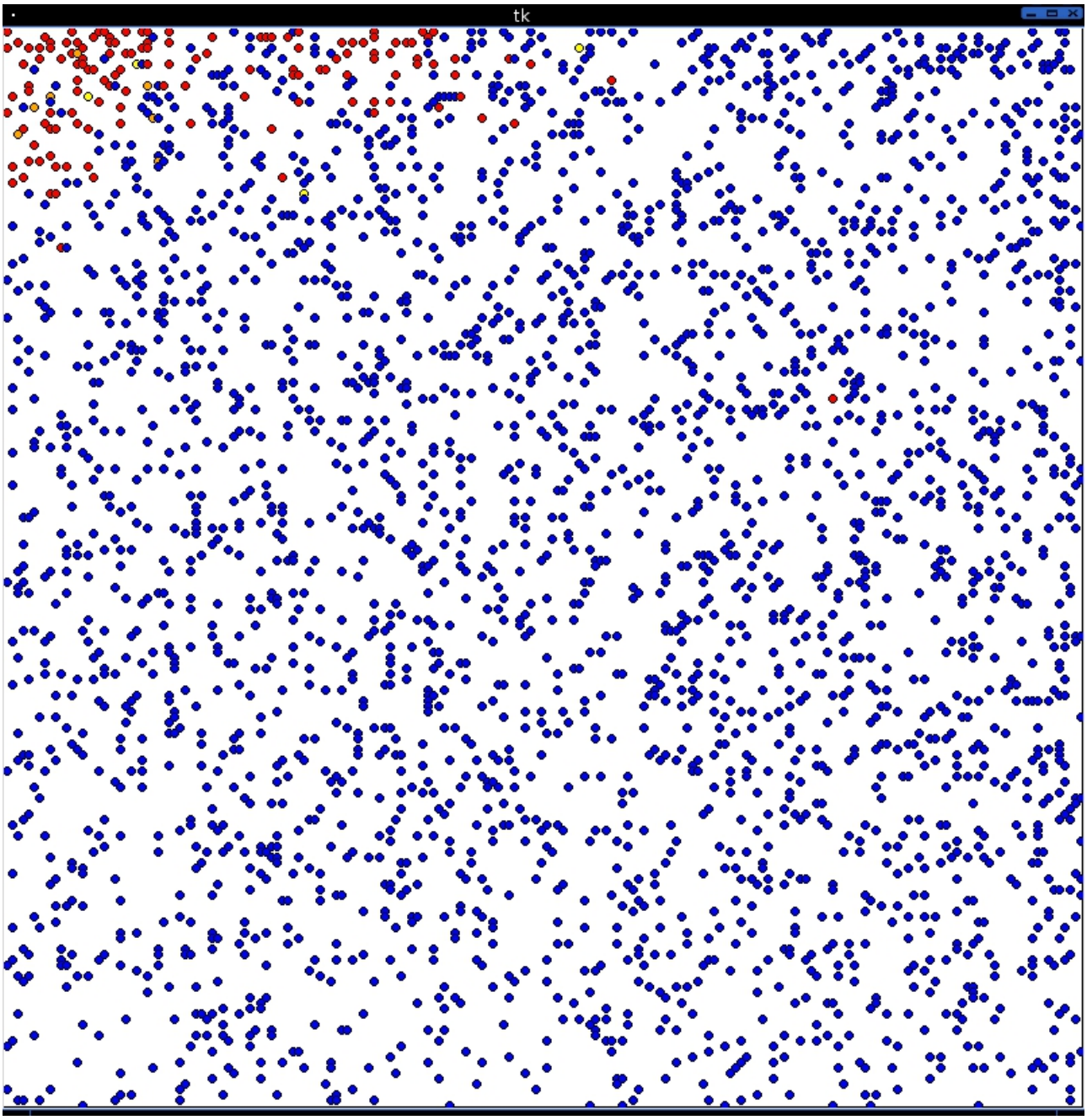
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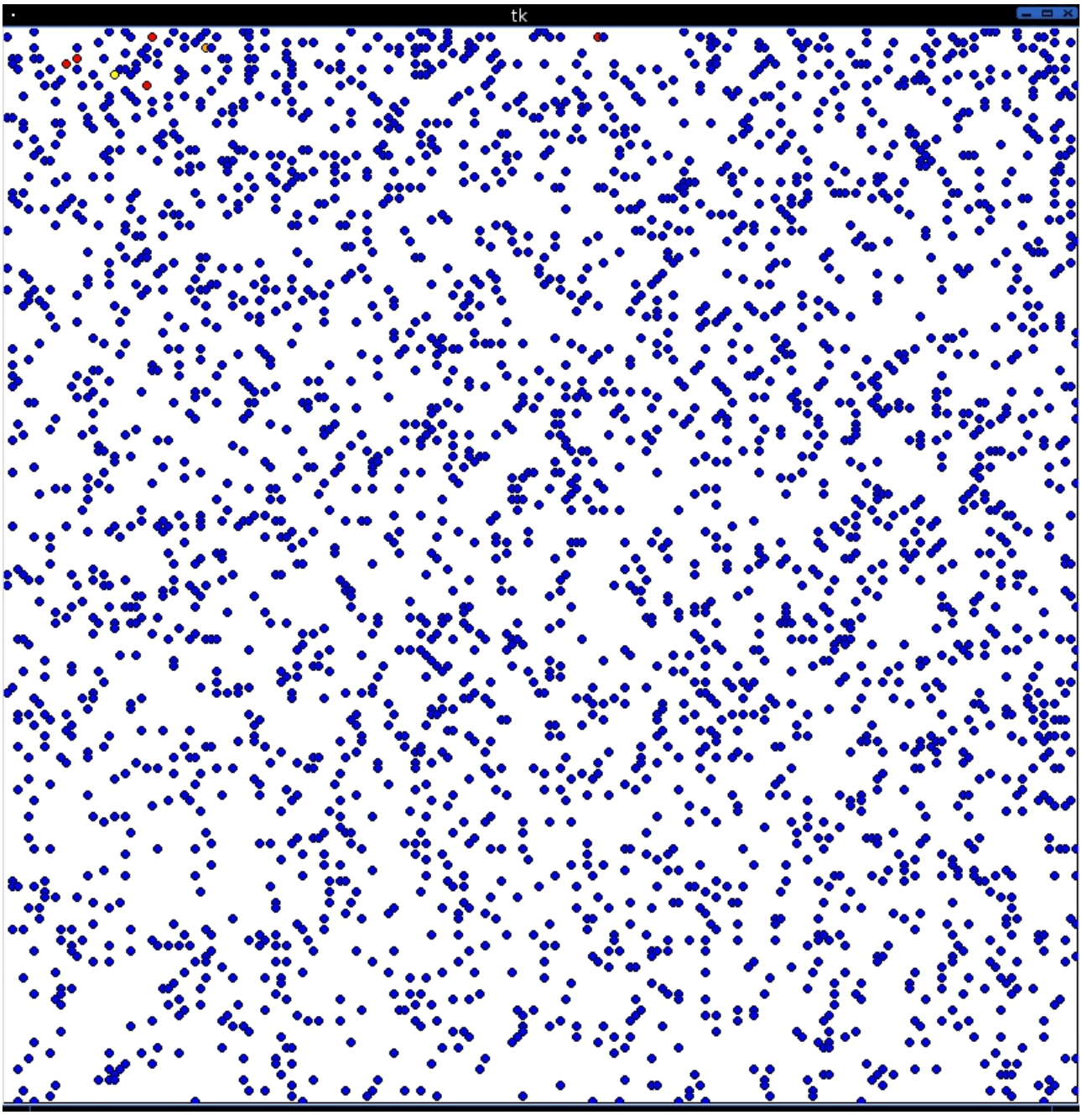
Trial	Healthy	Carriers	Prodrome	Infected	
1	0	0	1	6	
2	0	0	0	10	
3	0	0	0	0	
4	0	0	0	9	
5	0	0	0	0	
6	2	0	0	0	
7	0	3	2	73	
8	0	0	0	9	
9	0	0	0	0	
10	1	0	0	2	
Average	0.3	0.3	0.3	10.9	



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