24C3: Modelling Infectious Diseases in Virtual Realities
The „Corrupted Blood" plague of World of Warcraft TM from an epidemiological perspective
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I will begin with a brief introduction to modelling diseases, describe how I modelled the „corrupted blood" plague of the online game World of Warcraft and finish with a few ideas on future virtual epidemics.

Epidemiological modelling primer

SIR model

Epidemiology is the study of the pattern of disease in time, place and population. Very often, the goal is to identify the underlying causative factors of disease. One of the early epidemiological successes was the discovery by John Snow of contaminated water pipes as the underlying cause for the great London Cholera epidemic in 1854. Another well known example is the link between smoking and lung cancer.
Infectious diseases as opposed to chronic diseases are somewhat unique in epidemiology because exposure and outcome are the same: an infected person (or animal in case of zoonoses). This leads to non-linear dynamics that make analysis and prediction of infections in a population very challenging.
One approach is to simulate the epidemic in a mathematical model that describes the relationship between sick and healthy people in order to test different interventions.
There are many ways to design a model. Individual or agent based systems allow for single individuals with their distinct characteristics like age, sex, contact pattern, risk taking and healthcare seeking behaviour, etc. These "agents" are then put into a simulation and the spread of disease within the population of agents is observed. Of course, all system parameters have to estimated from real world data, which can be very difficult or in the words of J. Maynard Smith: „Describing complex, poorly-understood reality with a complex, poorly understood model is not progress".
Another modelling paradigm are compartimental models which divide the population into distinct compartments of susceptible to disease (S), infectious (I) and recovered (R), where recovered are considered to have acquired immunity. These SIR models (Kermack-McKendrick 1927) assume homogenous mixing within the compartments, i.e. they imply that all susceptibles have the same probability to meet infectious. This assumption is like most other modelling assumption always wrong, but what matters is the strength of violation. In most cases, the SIR model and its variants are adequate.

The challenge with a SIR model is to estimate the flow between different compartments, most notably between S(usceptibles) and I(nfetious), which will be explained in more detail. For simplicity, birth rate and natural death rate are ignored (closed population).
Assuming homogenous mixing, the overall contact rate is `c`. Since we are only interested in contacting infectious, we multiply with the proportion of infected `I/N` (where N=S+I+R = total population).
However, meeting with an infectious does not always result in an infection event. This only happens with a transmission probability `p`. For tuberculosis for example, one would have to meet approximately 20 infectious people before contracting the disease whereas measles or Ebola have a transmission probability close to one. The term `p*c` is also called „beta" or "force of infection".
So far, we have `p*c*I/N` which corresponds to the rate of transmission from infectious. The total transmission rate in a population is the number of susceptibles `S` multiplied by that rate, finally yielding `p*c*I/N*S`. N, p, c are constants, S and I are state variables and change with time, making the whole system non-linear as mentioned above.
The "flow" from compartment I to R is simply the inverse of the duration of infectiousness (D), usually called delta. For example, if one remains infectious for 10 days (D=10) and time is counted in days, then 1/10 per day (1/D) of I flows to R. However, compartment I also looses individuals due to death at the disease specific death rate sigma. Here, sigma is set to zero.
Summing up, compartment S "looses" individuals at a rate of `p*c*I/N*S`, compartment I gains individuals at that rate but looses individuals at rate delta to compartment R. Compartment R gains individuals at rate delta.
These rates are put into a system of differential equations which are solved numerically by computer programs such as Berkeley Madonna (http://www.berkeleymadonna.com/).
In formula (dS/dt means change of S over time, no birth rate, no natural or disease specific death rate):

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dS/dt = -p*c*I/N*S
dI/dt = p*c*I/N*S - delta*I
dR/dt = delta*I
```

The SIR model is suited for infections that generate immunity (R compartment). If immunity is lost with time, one would use a SIRS model where the „waning immunity" rate would determine the „flow" from compartment R to compartment S back again.
Most sexually transmitted infections such as syphilis, gonorrhoea or chlamydiasis but also the „winter vomiting disease" caused by Norovirus generate no or only partial immunity. S(usceptible) become I(nfectious) and after curing the infection S(usceptible) again, resulting in a SIS model. Diseases such as Hepatitis C or HIV (!condoms protect!) cannot be cured and leaves people I(nfectious), yielding a SI model.

The basic reproductive number R0

R0 („R naught", „R zero") is the average number of secondary infections from one single infected in a totally susceptible population. This is the same as asking: „how many people does one infectious person infect if everybody is susceptible ?". If R0 is below one, the epidemic dies out.
R0 is the product of mean duration of infectiousness (D), contact rate (c) and transmission probability (p):

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R0 = D*c*p
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The concept of R0 allows to assess the impact of different epidemic interventions. Quarantine for example reduces the contact rate whereas treatment would act on duration of disease and/or transmission probability. Tamiflu for influenza e.g. shortens period of infectivity (D) and inhibits viral shedding (p). Wearing face masks would inhibit spread of airborne infections (reduce p) and rigid hand hygiene would greatly reduce any fecal oral transmission (reduce p).
Sometimes, interventions or social customs can also increase R0. If an intervention prolongs duration of disease or increases p, the epidemic gets worse. For example, in the beginning of the SARS epidemic, patients were treated with steam-nebulisers to ease breathing. However, additional aerosolisation of airborne infections is really the last thing you need during an epidemic.

Corrupted Blood

Hakkar the Soulflayer

On September the 13th, Blizzard Entertainment released new gaming content for their acclaimed massively multiplayer online roleplaying game, „World of Warcraft" (WoW). For the sake of brevity, basic knowledge about WoW is assumed.
A new map region called „Zul Gurub" with a new challenging end-game opponent „Hakkar the Soulflayer" were waiting for high level players. During battle, Hakkar cast a spell called „corrupted blood" (CB) on a random player that hit with severe damage once and additional smaller damage over time (DOT). DOT-spell are not uncommon in Wow, however totally new was the ability of the spell to get „transmitted" to nearby players and their „pets" (fighting companions). The spell was infectious. The original intention of the game designers might have been to force players to spread over an area and thus let the infection run out by eliminating contact between players. What happened was that once infected player teleported back to populated cities or hunters (special classes) summoned back their infected pets, CB spread like the famous black death and depopulated whole areas. Worse still, non player characters like in-game shopkeepers or guards got infected as well. The game designers first tried to quarantine the disease but ultimately failed and had to shut down the virtual world and reload it with a non-infectious version of CB. The CB-incident caught a lot of media attention and fuelled discussion on using online games as epidemic simulators.

Modelling CB

First, it has to be said that any epidemiological modeller could have predicted the devastating effects of CB. The basic reproductive rate R0 was so absurdly high, that any natural pathogen would have killed its host population and thereby sealed its own fate: no host, no pathogen.
Model parameters usually have to be estimated from observational data. To the great dismay of the epidemiological community, no observational data on CB incidence is available from Blizzard. However, with a programmed disease like CB, parameters are available directly. Duration of the disease, providing survival, was 10 seconds. Low and mid level players died after two hits by the disease that was 4 seconds. Transmission probability was one, that is everyone in vicinity of an infectious got infected as well. Not even

Ebola is that contagious. Contact rate depended on geographic location. In special WoW meeting places in cities like the auction house, a contact rate of 5 players per second is not uncommon. Outside cities, contact rate was lower.

Low/Mid Level Avatars
Death in WoW is non-permanent: killed players become ghosts on a graveyard and can eventually resurrect later. In terms of modelling this translates into a SIRS model for low-mid level players: S(usceptibles) become I(nfectious) and by „dying“ enter the R(ecovered) compartment, only to „resurrect“ and become S(usceblible) again (fig. 1).

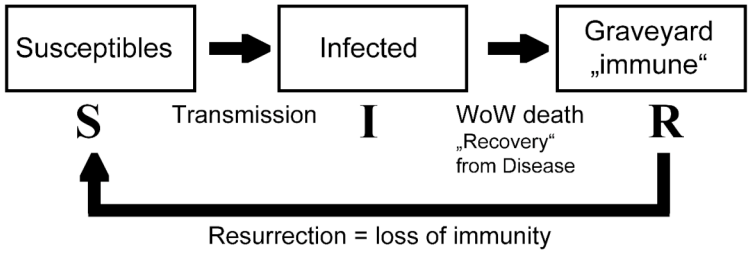

Figure 1: SIRS model

It might seem confusing to think of dead players as recovered, but in terms of disease modelling, they cannot be infected while on the graveyard and are thus, for the sake of CB, recovered.

The graphs in fig. 2 illustrate the course of the epidemic with different contact rates.
A: one infected at start, contact rate 2/s, resulting in 85% of players wasting their subscription fee on the graveyard with a slightly diminished in-game experience.
B: 500 infected at start, contact rate 1/5s, epidemic dies out because of R0= D*c*p=4*1/5*1, which is <1. In words, each infected creates less than one secondary infection.

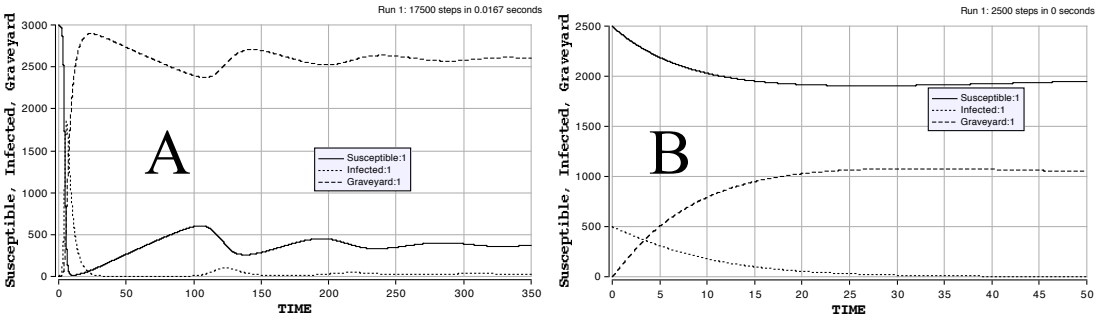

Figure 2: SIRS dynamics depending on contact rate. Susceptible black, infectious thin dotted, recovered thick dotted

High Level Avatars
High level avatars survive CB. They “bounce” back between S(usceptible) and I(nfectious) and are modelled using a SIS-model (fig. 3).

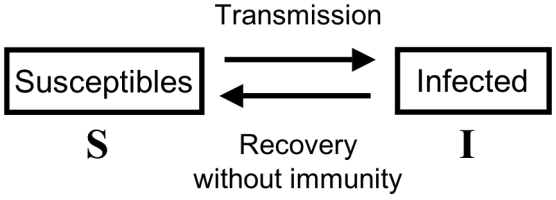

Figure 3: SIS model

The graphs in fig. 4 illustrate the course of the epidemic with different contact rates.
C: one infected at start, contact rate 2/s, resulting in 95% of players staying infectious.
D: 500 infected at start, contact rate 1/20s, epidemic dies out because of R0= D*c*p=10*1/20*1, which is <1 (D is 10 seconds and not 4 as in the SIRS cases A and B, as high level Avatars survive the full duration of the spell).

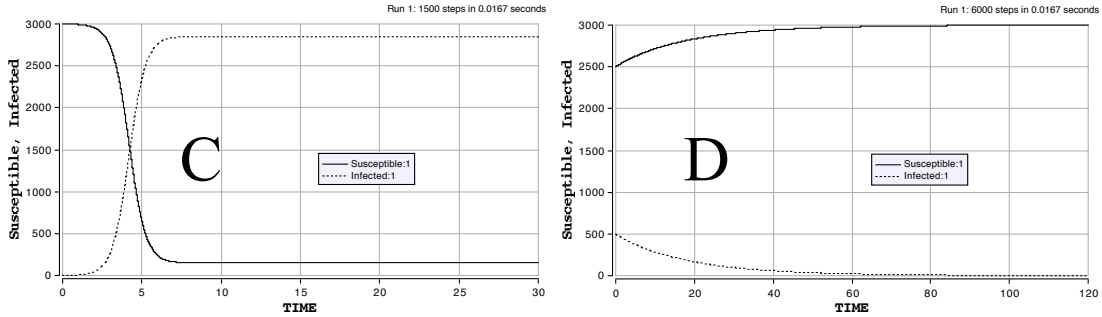

Figure 4: SIS dynamics depending on contact rate; susceptibles black, infectious dotted

Better virtual epidemics

Game designers should take a few cues from nature when introducing infections in virtual worlds. A transmission matrix with different transmission probabilities between races would allow more detailed modelling of interspecies infections (why should an orc-virus infect elves and vice versa?). Transmission could also depend on age and sex. And please note: transmission probability is never one, not even for Ebola or Measles.
Recovery could be made time dependent, i.e. avatars stay infectious for a random length of time.
Introduction of immunity would limit the devastating effects that were seen with CB. Immunity could gradually disappear thus simulating genetic changes in the infectious agent, which is seen with influenza. Immunity would also add the possibility of biological warfare, if eg. immune Alliance players including one infected would raid a susceptible orcish village. That strategy would mirror the distribution of smallpox contaminated blankets to Native American Indians in the 19th century. Immunity would also add vaccination as a service that might be synchronised with real-world flu-jabs.
Addition of an incubation period, where people are infected but not yet infectious, would more closely resemble real diseases.
Transmission routes could vary as well: food-borne, airborne (droplet infection) or injury just to name a few (with all those nasty cuts and flesh wounds in WoW, one wonders why there are not more wound infections...).
Online avatars are probably in no danger of sexually transmitted diseases any time soon.

Links & References

- Short course on epidemiology of infectious diseases, http://www.imperial.ac.uk/cpd/epidemiology/
- The untapped potential of virtual game worlds to shed light on real world epidemics, Lofgren ET, Fefferman NH, Lancet Infect Dis 2007; 7:625-29
- Berkeley Madonna, http://www.berkeleymadonna.com/
- Corrupted Blood, Wikipedia, accessed 16.11.2007, http://en.wikipedia.org/wiki/Corrupted_Blood
- Bapf the „Master Sergeant“
- presentation and paper available at http://www.burckhardt.de/docs.html