Some Remarks about the Complexity of Epidemics Management

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Abstract

Recent outbreaks of Ebola, H1N1 and other infectious diseases have shown that the assumptions underlying the established theory of epidemics management are too idealistic. For an improvement of procedures and organizations involved in fighting epidemics, extended models of epidemics management are required. The necessary extensions consist in a representation of the management loop and the potential frictions influencing the loop. The effects of the nondeterministic frictions can be taken into account by including the measures of robustness and risk in the assessment of management options. Thus, besides of the increased structural complexity resulting from the model extensions, the computational complexity of the task of epidemics management — interpreted as an optimization problem — is increased as well. This is a serious obstacle for analyzing the model and may require an additional preprocessing enabling a simplification of the analysis process. The paper closes with an outlook discussing some forthcoming problems.

1 Introduction

1.1 Threats by Epidemics

Sometimes, epidemics management turns out to be unsuccessful. The plague pandemics in the middle ages, for example, were not handled effectively [17, 49]. We have learned much in the meantime. Despite of all medical progress, however, the recent outbreak of H1N1 [11, 51, 81, 82] and other infectious diseases made clear that biological contagions are still a significant threat. The recent Ebola epidemics [50, 70] has shown, that even a known pathogen can go out of control easily [54]. The recent series of sporadic cases of infectious illnesses [13] is the reason why epidemics research is still of high actual importance [36]. This threat will persist in the future, eventually even increasing due to a variety of effects including evolution of relevant contagions, climate and ecosystem change, land use, and increasing travel activities [36].

1.2 Frictions as Threat Multipliers

The events mentioned in the introduction have shown the vulnerability of industrial nations against the threat of known and unknown epidemics. This has led to the development of various methods for mitigating epidemics effects in order to avoid catastrophic developments. Processes and organizations have been established with the intention in mind to fight infectious diseases effectively. Despite of all these efforts, epidemics management have been confronted with mishaps and unforeseen problems with potentially dramatic consequences. For naming but a few examples:
Figure 1: Graphical representation of an idealized epidemics management process as used in traditional approaches to epidemics management.

- The substandard gear used by a Spanish nurse was held responsible for infecting her with Ebola [33].
- Laboratories reported more than 230 safety incidents with bioterror viruses and bacteria in 2015 [79].
- In 2014, Ebola virus material from a BSL-4 lab leaked out of the lab. Several people were exposed to the material [47].
- The handling of an U.S. Ebola patient violated many regulations [63]. As an example, it has been forgotten to process bedclothes of this patient as highly infectious material [16].
- An undertaker in Germany infected himself with Lassa fever after being in contact with the corpse of a Lassa patient who died earlier [87].
- Inefficient communication [31] [86] leads to delays in distributing decisions and important informations.
- Especially the deciders themselves, namely the politicians, provided a whole catalogue of lapses and errors [88].
- Even a known pathogen may show strongly varying properties. For example, Marburg virus [64] shows variations in lethality from 25% to 90% of the infected people [48] [64].
- Pathogens are undergoing evolution, leading to unknown and new, unexpected properties, as for example the 1918 influenza epidemic [51].

According to the examples given above, the management of outbreaks of infectious diseases quite often do not work as expected from the traditional theories of epidemics and epidemics management. Their idealistic assumptions are not necessarily valid in practice. Thus, it
seems plausible to include the different kinds of frictions in the considerations. Frictions will typically influence the dynamics of an epidemics outbreak in a more or less significant way. Despite of these effects, frictions do not seem to be discussed in the necessary depth up to now. The present paper intends to make a contribution for closing this gap. Methods for relaxing simplifying and idealistic assumptions in epidemics modeling are discussed.

The necessary extensions for a corresponding model will give almost inevitably a ‘complex’ model, whereby here the notion of complexity has to be understood in the informal sense. Accordingly, it can be expected that due to the pure size of the model, the number of influencing factors, and the number of involved disciplines the assurance of a high level of objectivity becomes a central aspect. This is done from the system theory and model analysis point of view. Eventual consequences for the medical point of view are not elaborated here.

1.3 Relevant Papers
Several papers are considering the interactions between epidemics and other areas of science potentially influencing the epidemics like economics [20], human behavior [1, 10, 55], psychology [23, 52, 68, 74], sociology and knowledge [24, 54, 67, 80], and others [58]. A slightly more complex situation is considered in [81]. The paper [14] gives another view on the complexity applied to epidemics modeling. An article supporting a holistic view is [60]. A really multidisciplinary perspective on the topic of epidemics or epidemics management seems to be still missing, however.

The statement made above holds for frictions as well. A representation of a broad range of frictions in a multidisciplinary context appears to be a gap in the literature up to now. In the contrary, the paper [71] shows the necessity of taking such frictions into consideration. A paper taking frictions into consideration at least at a rudimentary level is [72]. Delays as special kind of frictions are discussed in [10]. Uncertainties were taken into consideration based on fuzzy logic in [42], but not by a probability-based representation in a simulation model as proposed here.

1.4 Structure of the Paper
In section 2 we analyze the consequences of an inclusion of frictions, uncertainties and other aspects of nonideality for the system under consideration. The analysis is done both from the structure and dynamics perspective. Based on these results, we derive in the following section 3 stochastic, genericity, and dynamics as basic requirements for a model suitably representing such a system. As it turns out, an extension of the compartmental modeling approach can be considered as appropriate modeling paradigm. Using this paradigm, section 4 discusses the computational complexity of the epidemics management task. One can safely state, that the computational complexity of task for a fully fledged model will usually be not tractable in practice. Measures of complexity reduction are necessary for making the problem feasible. The paper closes with a short outlook in section 5 summarizing the results and showing options for a future development of the topic.

2 The System of Epidemics Management
For discussing the epidemics management problems we will consider epidemics management as a system. The exploration of this system provides important informations about its properties.
They are used in the next situation for the decision about an appropriate modeling paradigm.

2.1 Representation of Influencing Areas

The mathematical modeling of epidemics and actions for their management has reached an advanced state [7, 28, 30]. The overwhelming majority of the scientific literature deals with idealized situations, however. If we want to provide a model which conveys the complications of epidemics management resulting from practice, it will be necessary to represent different kinds of frictions. In many cases this intention will lead to an ambitious project, because it may require the modeling of both the influences causing frictions as well as the organizational processes for resolving them. These model extensions have to be integrated with the epidemics management core model and will lead almost inevitably to a multidisciplinary model describing the relationships, interactions, and collaboration between many epidemics-relevant disciplines [37, 39]. Let us take a look at the diversity of potentially epidemics-relevant disciplines as seen in figure 2.
• Ecology may become important as soon as hosts and vectors are important for spreading a disease [22, 73].

• Climate may have a significant influence on the spreading of an epidemics [18, 29].

• Sociological aspects like traditional practices and burial rites [70, 83] are influencing the infection rate.

• Logistics and infrastructure are important e.g. for distributing vaccination sets and transporting infected persons (and infectious material) to hospitals and quarantine units [21].

• Politics, including different handling of different ethnic groups, opportunism, and corruption [88], is involved at the global level. In effect, politics may also be responsible for wars; actually, Syrian civil war is taking place causing streams of refugees. The refugees may be ill, eventually triggering epidemics or help spreading them [2, 61]. Furthermore, governments are responsible for a suitable preparedness and a suitable execution of epidemics management actions.

• The administration defines regulations, gives advice, and provides resources, which are usually limited.

• International Relationships in both political and medical respect may influence the admissible or demanded management actions.

• Psychology [25, 59, 70, 84] make humans react in different ways and not necessarily according to the intended aims of epidemics management [26, 40, 55].

• The economy is typically sensitively influenced by epidemics, since infected people do not belong to the workforce anymore [83].
  
  – The costs even of common influenza are enormous [44]. For the United States, the medical resp. overall costs amount to $10.4 resp. $87.1 billion in 2003.
  
  – The recent Ebola epidemics [27, 83] was causing a transition from economic growth to recession in some African states [45].

Besides of that, the limited resource of money is usually restricting the possible actions against an epidemics.

• Religion may have a strong influence (e.g. concerning usage of condoms) on sexually transmitted epidemics [62]. Sometimes, vaccinations are rejected due to religious reasons as well [46]. Another example were the fears of spreading MERS during hajj and pilgrimage in Saudi Arabia 2014 [38]. Insofar, religion is considered as item of its own, though it belongs in principle to the discipline of sociology.

Taking this diversity of additional influences into account and giving up the idealizations of classical epidemics management leads to a realization of a multidisciplinary model, which will in turn typically give a model with significant structural complexity.

Furthermore, we can state here about the influences on the epidemics system. Even worldwide organizations exist with the responsibility for handling epidemics as for example the WHO, but they can make only recommendations. They are not in the position to enforce
Figure 3: A seemingly elementary process like the identification of the disease of an infected patient may have a considerable complexity in reality. The picture shows the proposed organization for handling suspected Ebola cases in Germany according to [85]. The numerous persons involved in the identification process of the disease and the transport of and work with maybe highly infectious material have the potential to produce many additional infections in the case of severe mishaps. Furthermore, the information exchange between the various institutions may be subject to disturbances. The high potential for the occurrence of faults and mishaps makes it advisable to include such processes in a realistic model of epidemics management.

any kind of regulations. Low-level deciders like family doctors, on the other hand, may have a decisive influence on epidemics dynamics especially in the outbreak phase. A single mishap at the single-person level — say a person with a highly infectious disease not recognized by a physician — may be amplified by epidemics spreading across the population to a system-wide problem. Summing up, we are considering a multi-scale system here.

2.2 Representation of Dynamic Processes

A system is not only characterized by its structural properties, but also by its dynamical characteristics. For an adequate representation of the corresponding processes in a model, the main components involved in such processes must be included. As an example of such a process, consider the process describing the identification of an illness (see figure 3) with the special case of Ebola in mind.

We will consider another example from a slightly different perspective. Sometimes, flow
parameters determining system dynamics are influenced by a large spectra of factors. In first approximation, the infection rate $\beta$ is determined by the infectivity of the disease and the contact behavior between susceptible and infected persons. This situation in the traditional epidemics management may look different when considered from a more detailed perspective (see figure 4).

The two examples given above adumbrate that the dynamics of epidemics management is complex and cannot be described by a simple formula. Indeed, when taking a closer look one will be able to identify many feedback loops:

- Parts of the population are needed for executing epidemics management actions. Since people exercising their job become more and more rare during a serious epidemics, it will be hard to realize the intended countermeasures at some point.
- Obviously, frictions, countermeasures considered as inefficient, or an epidemics seemingly out of control may easily cause strong emotions like mistrust or fear in the public. This, in turn, can lead to additional infections due to phenomena like circumventing control points, rejection of vaccinations, mass flight, or violating quarantine regulations.
- An epidemics insurance [27, 89] intends to mitigate the epidemics effects by providing the resources necessary for fighting it. Recognizing the reduction of risks by the insurance, the insurance taker may be tempted to reduce own preventive measures.

Besides of feedback loops, the epidemics management system contains trade-offs as well. In such a case, some of the various factors influencing epidemics management are compensating each other. Take for example the question when to start countermeasures. An early start of countermeasures will fight the outbreak more effectively. Due to possible disadvantages like medical problems caused by vaccinations, or the restrictions of personal freedom associated with quarantine regulations, the population may partially reject early countermeasures especially in the case of initially low infection numbers. In general, the presence of a trade-off means that typically not even the tendency of system reaction can be predicted. Perturbations may be amplified as well as damped out.

2.3 Representation of Friction Effects

There is a large spectrum of different kinds of frictions [21, 24, 70] as shown in figure 5. Human factors, delays unknown in advance, and unexpected events are occurring. Informations about epidemics are becoming available only time after time. Furthermore, epidemics management is error-prone in principle due to its distributed character. Various mistakes can occur during measurement, communication, collaboration and so on between the individual control components. Since these frictions may have a decisive disadvantageous influence on the outcome of epidemics management [59, 70], their inclusion seems to be mandatory as soon as a realistic view on the management process is intended. The following list gives a taxonomy of important friction classes together with some explanatory notes.

Stochastic Variations, Noise, and Frictions: In principle, the epidemics management process can be disturbed by different kinds of noise anywhere and anytime. The noise may be represented by stochastic variations leading to erroneous observations results, inadvertently set action parameters, inadequate decisions, unforeseen delays, and additional waiting times.
Figure 4: The vaccination rate $\delta$ is not only determined by the capabilities of executing a vaccinations, but also by available vaccination sets. They may be at hand in the stocks, provided by donations and bought using money coming from the government, international aid, or a bio-insurance. Taking such influences into consideration is important for assessing the effectiveness of vaccination as epidemics management action.

**Observables:** Some observable data may be inaccessible or missing. The pathogen causing an epidemics may neither always be identified without doubt nor may have always known properties. Especially in their early stages, misidentification of exotic illnesses are quite common. A prominent example is the similarity between the symptoms of an early stage of an infection by viral hemorrhagic fevers and of an influenza infection [63].

**Multiple Players:** All these players have their own interests and aims and trying to realize their own plans. Thus, each authority may make its own decisions. This may include counteracting the actions of epidemics management. HIV can serve as an example. Whereas health organizations all over the world recommended to use condoms as a protective measure, the pope voted against it due to religious reasons. For many people in Africa, the pope was the higher authority resulting in dramatic consequences for the developing HIV epidemics in Africa [62]. The existence of other players may produce large deviations.

**Constraints:** Selection and application of control actions are prominently influenced by con-
straints. These constraints include the limitation of the available resources like medical equipment or mosquito nets and of the possible execution rates of management actions like vaccinations. Thus, they indirectly influence various parameters of the epidemics dynamics.

Evaluations: The assessment of the effects of epidemics and epidemics management can be varied in manifold ways. For example, the set SF36 is a collection of 36 items relevant to physiology and psychology. Another standardized set of evaluation measures for medicine is PGWB consisting of 22 psychological relevant items. The evaluation task is further complicated by different personalities and individual perspectives of the analysts, which induces some kind of subjectivism. Even applying an evaluation measure at different simulation times may assess different aspects like immediate epidemics effects vs. long-term-effects. For naming examples, consider the immediate impact on the gnp caused by the workforce drop-out vs. the cancelation of economic investments. Since the different evaluation measures are typically incomparable to each other, a multiple-criteria evaluation will result.

Actions: The dynamics of the epidemics can be influenced by epidemics management actions. Their execution times and parameterizations are determined by the decisions of epidemics management.

3 Models of Epidemics Management

3.1 Requirements for the Modeling Paradigm

Now, we are going to derive a modeling mechanism, which can represent the epidemics management system considering our findings about the underlying system characteristics. This means that the model must be able to handle the existing structural and dynamical complexity.

At first, we can state immediately that an appropriate model must be stochastic for representing frictions having a statistic nature as stated in section 2.3. The simplifications contained in the model are another source of stochastic behavior, which are inevitable for abstracting from the unbounded complications of the real world. The explicit details of the system omitted in the model are transformed to implicit stochastic fluctuations.

Second, the counteracting influences of the epidemics and of the epidemics management actions together with other complications as indicated in section 2.2 — feedback loops and trade-offs — gives the overall system representing epidemics management a complex dynamics. A maybe continuous inflow of supplementary informations for the system components responsible for epidemics management and sporadically occurring unexpected events will require an ongoing adaption of the intended control actions to the actual situation. Both factors, a complex dynamics and ongoing modifications of the course of actions, make an explicit representation of temporal aspects mandatory. This is done by pursuing a simulation-based analysis of the model.

Third, the choice of the model representing the epidemics system may quite often be subject to debate. A change of the available level of informations may require adaptations of the model. Different stakeholders may want to analyze the system with different aims in mind requiring somewhat different models. The deviations between the models may concern the model parameters, the addition of hosts, resources, and vectors, the reproduction of ecological subsystems, or the epidemics submodel (e.g. SIR-type vs. SEIR-type). In order to assure
some kind of comparability of the results provided by different models, these models should have a common generic structure.

3.2 Compartmental Modeling Paradigm

Summing up the contents of the last section, an adequate modeling paradigm provides stochastic simulation models with generic structure. Compartmental models \( SIR \) are suitable candidates. As illustration, one can look at the equation system describing the basic SIR epidemics model

\[
\begin{align*}
    \frac{dS}{dt} &= -\beta I \cdot S / (S + I + R) & S(0) &\geq 0 \\
    \frac{dI}{dt} &= \beta I \cdot S / (S + I + R) - \gamma I & I(0) &\geq 0 \\
    \frac{dR}{dt} &= \gamma I & R(0) &\geq 0
\end{align*}
\]
wherein the parameters and variables have the following meaning:

| Symbol | Meaning                        |
|--------|--------------------------------|
| $S$    | Susceptibles                   |
| $I$    | Infectives                     |
| $R$    | Recovered people with immunity |
| $\beta$ | Contact rate                  |
| $1/\gamma$ | Average infectious period |

As seen in equation (1), compartmental models have an explicit time dependence due to their equivalence to a differential resp. difference equation. Consequently, the dynamic behavior of the model can be analyzed by a simulation of the model. Stochastic variations can be included without any problem. Furthermore, compartmental models are generic as well. They represent the state of the illness in the population by the portion of people being e.g. susceptible, infected, or recovered. This concept can be generalized to other attributes like age, sex, job, hygienic standards, membership to risk groups etc. A corresponding example describing a quite complex situation involving humans, several vectors and several hosts is given by the plague [17, 49]. This flexibility allows to represent system structures as shown in the figures 2, 3, and 4.

### 3.3 Compartmental Models on Networks

The flexibility of the compartmental modeling paradigm allows to distinguish different sub-populations provided with individual epidemics parameters. This could be realized by using a network $G = (V, E)$ [73, 78], in which the nodes $V = \{v_i\}_{i \in I}$ of the network correspond to the different subpopulations, whereas the edges $E = \{e_j\}_{j \in J}$ with $e_j = (v_i, v_k) \subseteq V \times V$ correspond to interactions between them [4, 12, 15, 41]. This leads to an epidemics dynamics described by the equation system

\[
\begin{align*}
\frac{dS_i}{dt} &= -\beta_i I_i S_i / (S_i + I_i + R_i) + \sum_{k \in I, k \neq i} \tau^S_{ik}(t) S_k \quad S_i(0) \geq 0 \\
\frac{dI_i}{dt} &= \beta_i I_i S_i / (S_i + I_i + R_i) - \gamma_i I_i + \sum_{k \in I, k \neq i} \tau^I_{ik}(t) I_k \quad I_i(0) \geq 0 \\
\frac{dR_i}{dt} &= \gamma_i I_i + \sum_{k \in I, k \neq i} \tau^R_{ik}(t) R_k \quad R_i(0) \geq 0
\end{align*}
\]

(2)

In the set of equations given above, an index $i$ indicate that the corresponding object belongs to the node $v_i \in V$. The flow from the node $v_i$ to the node $v_k$ for susceptible, infected, and recovered persons are described by the time-dependent flow parameters $1 \geq \tau^S_{ik}(t)$, $\tau^I_{ik}(t)$, $\tau^R_{ik}(t) \geq 0$. Supplementary constraints on the flow parameters assure that the size of the overall population remains constant over time. The equation system (2) is more complex than (1), but can describe specific situations more precisely by e.g. locally modified epidemics parameters. This may improve the prediction accuracy.

The compartment approach has the capability of representing single persons in principle. Since the behavior of single persons may influence the outcome of the epidemics significantly, such a high resolution view seems to be advantageous according to the observed multi-scale property of the epidemics system. An agent-based model representing all individuals of a densely populated nation is intractable from the computational complexity point of view, however.

A decisive advantage of the network approach in this respect is the freedom to represent a given situation in different resolutions. A whole national state can be modeled as a single SIR model, as a network of federal states with edges as neighbourhood relations, as a network...
of roads between towns, villages, airports, hospitals etc. and so on. This makes it possible to adapt the model to the available computing power and the restricted availability of data. It does not make sense to use a highly detailed model if the many parameters of such a model can not be given specific values by the available data.

Figure 6: Compartmental model defined on a network representing a situation consisting of a small camp \( C \) and a large town \( T \). Epidemics in \( C \) or \( T \) is described by a traditional SIR model. Camp and town are connected by a road \( W \), giving a network \( G = (V, E) \) consisting of the nodes \( V = \{v_C, v_T\} \) and the edge \( E = \{W\} \) with \( W = (v_C, v_T) \). People are moving from the camp \( C \) to the town \( T \) as described by the flow parameters \( \tau^S_{CT}(t), \tau^I_{CT}(t), \tau^R_{CT}(t) \).

3.4 Compartmental Models with Control Components

Compartmental models are a kind of graphical representation of a system of differential resp. difference equations. Such a modeling approach can describe epidemics dynamics and epidemics effects on the population, but it is not considered as appropriate for epidemics management. A management process typically involves decisions about a finite number of management actions contrary to the continuous world of compartment models. Such decisions are typically made based on logical conditions over observation data. Thus, we have to supplement the modeling paradigm of compartmental models \[7\] with a paradigm capable of representing logical reasoning \[19, 57\]. Similar constructions were used in \[5, 66\]. Formally, decision makers are represented as control components, which are executing observations, make decisions, and schedule epidemics management actions as depicted in figure 7. More detailed, a control component works in the following way.

The state \( q(t) \in Q \) of the epidemics system at time \( t \) is narrowed down by a control compartment using observations \( o:Q \to O \). The domain \( O \) of the observations \( o \) may for example concern the levels of compartments. Ideally, they allow a precise determination of \( q(t) \); in reality, usually only a subspace \( Q' \subseteq Q \) of \( Q \) is observable. The informations about \( q(t) \) provided by the observations \( o(q(t)) \) are used in a decision strategy \( D:O \to A \) for creating a plan \( A \) intended to mitigate the epidemics. The plan \( A \) consists of epidemics management actions like vaccinations, information campaigns, calls for social distancing etc. to be executed at times \( t' \geq t \). These actions may be parameterized accordingly for adapting to specific infection rates, vaccination capabilities, available quarantine facilities etc.

The ‘final’ outcome of a plan \( A \) with respect to a time horizon \( H \) is evaluated using an assessment function \( c(q(H)) \) applied on the state \( q(H) \in Q \) reached by the system at the
time horizon $H$; the horizon $H$ determines the time interval $[t, H]$ covered by the prognosis of the outcome. Interpreting the assessment function $c$ as cost function, the control component pursues ‘minimal’ values of $c(q(H))$ characterized by conditions like a vanishing number of infected persons, very few persons killed by the epidemics, low economical impact and so on. The evaluation measure $c$ defines the aim of the control component, which selects a plan $A$ influencing the dynamics of the epidemics (hopefully) in such a way, that the outcome $q(H)$ after applying $A$ on $q$ is indeed minimizing $c(q(H))$ over the set of all epidemics management plans.

3.5 Compartmental Models with Friction Effects

As deduced in section 2.3 frictions affecting epidemics management — i.e. the control loop — should be included in epidemics models aiming at a more realistic model behavior. In the following, we discuss how the different types of frictions identified in section 2.3 can be represented in the model.

*Stochastic Variations:* Stochastic noise is a very prominent type of frictions affecting both input and internal system parameters. It can be represented in the model as random variable influencing the parameter value. The noise characteristics is determined by the stochastic distributions assigned to the random variable and the function modeling the influence on the parameter value (say, addition or multiplication). Moreover, stochastics may be also used for handling uncertain or even completely unknown model parameters. Such uncertainties subsume a variety of semantically different effects, which may all be described in the framework of stochastics. Typically, one may distinguish uncertainties of measurements, parameters, and stochastics.

*Multiple Players:* As mentioned before, epidemics management is characterized as a distributed control consisting of persons with own interests and a variety of organizations with not well-defined responsibilities. Consequently, the actual epidemics situation may be influenced by actions of multiple players. The usage of specific observables and actions, the dependence on the ‘personality’ of the decider, and phenomena like limited rationality take part in the decision making process $D$. As an example of the effects resulting from these complications consider the example given in figure 6. As depicted, we are discussing a situation consisting of a camp $C$ and a town $T$ connected by a road $W$. If a person in the camp gets infected and an epidemics starts, epidemics management conducted by the government may aim at an containment of the epidemics in the camp $C$. Accordingly, the government may establish a check point at the road connecting $C$ and $T$ for blocking any traffic inbetween. The inhabitants of the camp, on the other hand, are in more and more danger of getting infected when the epidemics is developing in $C$. Being interested in their personal safety, the inhabitants are thus motivated to flee from the camp $C$ to the town $T$ for avoiding an infection. Doing so, they probably transfer the epidemics from $C$ to $T$ compromising the strategy of epidemics management. In effect, the decisions of parts of the population will thus counteract the decisions of the government.

*Constraints:* Limitation of rates and resources, rules coming from higher level components (e.g. politics), and other restrictions concerning the execution of management actions define a set $C$ of constraints on the selection of the strategy $D$. The constraints $C$ may change over time since e.g. additional resources can be produced and bought.
**Evaluations:** Usually, the evaluation measure $c$ is not a scalar, but a vector $c = (c_1(x), \ldots, c_k(x))$ of single objectives. Since it is not possible in the general to find a state $x$ optimizing all $c_j(x)$ simultaneously, one is typically confronted with a set of solution candidates. It is not obvious how to decide in such a case. Usually additional factors come into play at this point like preferences or risk attitude of the decider. These factors enable the decider to filter options and to compare the remaining choices with each other from her personal perspective allowing a decision at the end. Due to the interpretation of $c_j$ as some kind of cost function, in the following $c_j \geq 0$ is assumed.

![Principle Structure of the epidemics management control loop. Red text designates frictions of stochastic nature, whereas red background indicates frictions having global effects. Blue text indicates frictions with deterministic influence.](image)

4 Computational Complexity of Epidemics Management

4.1 Computational Complexity of Simulation-based Analysis

Epidemics management has a natural interest in the question, which management actions are suitable. This can be understood as an optimal planning problem concerning the actions to be scheduled for mitigating the epidemics effects in the best possible way. In the following, a simulation-based approach for solving this problem is given with $S^A_{H}(x)$ as system evolution function for the start state resp. parametrization $x$ from the start time to the time $t = H$ under inclusion of the scheduled actions $A$. Later, we will also use the notion $S^f_{H}(x)$ for the corresponding system evolution influenced by frictions $f$. 

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As mentioned in section 3.5, we must handle multicriteria evaluation measures \( c \). Using the abbreviation \( y := S_H^M(x) \), the optimization problem to be considered has the form

\[
\bar{x} := \min_{x=(x_1, \ldots, x_n) \in P} (c_1(y), \ldots, c_k(y)) \quad \text{with } P = \bigotimes_{i=1}^{n} I_i
\]

(3)

\( P \) designates the \( n \)-dimensional parameter space over which the optimization has to be executed. The evaluation measures \( c_1, \ldots, c_k \) are used as optimization objectives.

Unfortunately, non-smooth aspects make it difficult to predict the overall behavior of the system and give the optimization problem a combinatorial character. Two significant effects are contributing to the non-smoothness. First, the discrete decisions involved in the epidemics management process may induce non-differentiabilities in the evaluation measure components \( c_j \). Even discontinuities can not be excluded. Second, the optimization has to be executed over maybe less or even unstructured domains like the position of check points on the network of streets. This combinatorial character of the optimization problem is disadvantageous for the computational complexity [53], because one can usually not make use of an approximation process for finding the optimum anymore. An approximation relies on certain smoothness and continuity properties not necessarily given here. Without further knowledge about the behavior of the system there is no other way than to discretize the problem. One such approach consists of defining a grid covering the parameter space, making (3) computational in this way. The grid replaces the maybe continuous domains \( I_i \) by finite point sets \( I_i' \subseteq I_i \) providing a good coverage of \( I_i \). The modified optimization problem has the form

\[
\bar{x}' := \min_{x=(x_1, \ldots, x_n) \in P'} (c_1(y), \ldots, c_k(y)) \quad \text{with } P' = \bigotimes_{i=1}^{n} I_i'
\]

(4)

If the grid introduces \( m \) representative points for each of the \( n \) variables \( x_1, \ldots, x_n \), the grid will consist of a total of \( m^n \) points of support. If the grid is fine enough, the optimum \( \bar{x}' \) found on this grid can be assumed to be a viable approximation of the real optimum \( \bar{x} \) meaning \( \bar{x}' \approx \bar{x} \). Since the behavior of the system between the grid points is unknown and any attempt to reconstruct intermediate values from the data given for the points of support thus disputable, the validity of the assumed approximation property \( \bar{x}' \approx \bar{x} \) can not be guaranteed, however. The chances of being valid is increased by choosing a finer grid, though the higher number of simulation runs required for solving (3) on a finer grid is a limiting factor for a grid refinement.

4.2 Enabling a Simulation-based Analysis by Complexity Reduction

The optimization problem (3) is hard to solve because of the typically large number of system parameters. Furthermore, possible discontinuities e.g. due to decisions about management actions and the eventual presence of discrete aspects hamper the usage of approximation methods. Thus, one may be interested in methods for simplifying the optimization problem as long as they do not compromise the quality of the solution in an unacceptable way. Such a method is described in the following based on restricting the given optimization problem to the essential system parameters.

At first the system parameters \( x_i \) are ranked with respect to their importance for the optimization problem based on a sensitivity analysis. According to [77], a sensitivity assessment using an isolated analysis of the parameters \( x_i \) is attractive because of its simplicity. If we
assume that the domain $I_i$ of the $i$-th parameter $x_i$ is an interval $I_i = [a_i, b_i]$, this approach allows an immediate calculation of the sensitivity coefficients $s_i$ according to

$$s_i := \frac{S_H(b_i) - S_H(a_i)}{b_i - a_i}$$  \hfill (5)$$
as long as the variations of the outcome $S_H$ of the system evolution across $I_i$ is limited. When stronger variations occur, the simple measure of sensitivity given in (5) has to be replaced by expressions using additional points of support. In the case of many system parameters $x_i$, the combined handling of all $n$ variables using a design of experiment may be more effective. Though a full factorial design may still need $2^n$ points of support, a fractional design may scale down this number to $n + 1$ points of support corresponding to a computational complexity of order $O(n)$. This means a reduction of the number of simulation runs from the exponential to the linear scale, which makes the fractional design comparable to method (5) from the viewpoint of computational complexity. A more detailed discussion of sensitivity analysis applied to epidemics research can be found in [76].

Using the calculated sensitivity of the parameters $x_i$, we can now rank the $x_i$ according to their scale of influence on the system behavior. The ranking makes it possible to simplify the optimization problem (4) by restricting the parameter space $P$ to the subspace of parameters influencing the outcome sensitively. The other parameters are set to fixed values $x^0_j \in I'_j$. The choice of $x^0_j$ is uncritical because the parameter $x_j$ has no sensitive influence on $\bar{x}'$ according to construction. Let us assume w.r.o.g. that the indices $1, \ldots, n$ are already ordered according to the ranking and that only the first $n' \leq n$ parameters are included in the simplified optimization procedure. Consequently, the variables $x_{n'+1}, \ldots, x_n$ have to be set to fixed values $x_{n'+1}^0 \in I'_{n'+1}, \ldots, x_n^0 \in I'_n$. This gives the simplified optimization problem

$$\bar{x}'' := \min_{x=(x_1, \ldots, x_n, x_{n'+1}^0, \ldots, x_n^0) \in P''} (c_1(y), \ldots, c_k(y)) \quad \text{with} \quad P'' = \prod_{i=1}^{n'} I'_i$$  \hfill (6)$$

Since the parameters set to fixed values have low sensitivity, their variation would cause only small disturbances of the result. Thus, it presumably holds $\bar{x}'' \approx \bar{x}'$. Together with $\bar{x}' \approx \bar{x}$, this leads to $\bar{x}'' \approx \bar{x}$. The number $n'$ of parameters $x_i$ included in the simplified optimization problem (6) is a trade-off between the computational tractability of the optimization problem (6) and the quality of approximation of the full problem (3). It is expected that the parameters excluded from variation in (6) give only small corrections; thus they may refine but should not determine the solution. For validating the approximation property one can check whether the parameters $x_{n'+1}, \ldots, x_n$ excluded from the optimization process are indeed producing only small corrections. This can be done e.g. by executing corresponding Monte-Carlo runs.

### 4.3 Principle Strategy of Friction Analysis

The strategy described above can solve the basic optimization problem of epidemics management. We are continuing the considerations for the inclusion of frictions in the optimization process (see figure 5). Due to their fundamentally different character, we distinguish deterministic and nondeterministic frictions in the following. Many deterministic frictions can be included in the optimization problem without any change of the formalism. The constraints $C$ and effects of limited rationality, for example, are canonically represented by a modification
of the mapping $D$ describing the decision strategy. Not that clear is an appropriate strategy for the inclusion of nondeterministic frictions. We provide methods for handling stochastic disturbances representing noise and game-theoretic disturbances caused by different, not fully cooperative players.

Concerning stochastic noise, the various influences on the system dynamics are typically independent from each other and will thus usually lead only to local variations. Game-theoretic events, in the contrary, may be correlated. The existence of an ‘intelligent’ player following a distinct strategy may produce a ‘systematic’ deviation from the intended plan. This may provoke a \textit{globally} different solution, which is a fundamental difference to stochastics. A common property of both kinds of nondeterministic frictions is that ‘punctual’ considerations are inadequate. Instead, considerations based on simulation result families become of interest, whereby the members of such a family represent the different potential futures. Ongoing adaptations of the scheduled epidemics management actions for correcting unforeseen or unexpected developments and for taking additional and new informations into account are contributing to the variation of the outcomes.

The effects of nondeterministic frictions are quantified by risk and robustness measures assessing the effects of stochastic and game-theoretic variations. In effect, these measures can be handled analogous to the cost estimates provided by the evaluation measures $c_j$. Consequently, for including them in the optimization problem, the vector $c = (c_1, \ldots, c_k)$ of evaluation criteria is extended by the robustness and risk measures.

A remark is necessary concerning the risk measure. Risk is used here for characterizing global variations. Thus, one may be tempted to argue that risk is a property of the overall system and not a quantity assigned to individual points of support. In fact, however, the risk is calculated for a specific scenario associated with the point of support, which is typically determined by the action schedule for fighting the epidemics. The measured risk does not assess the possible disadvantages associated with the epidemics, but the possible disadvantages associated with a specific scenario. Thus, the risk is measured at each point of support.

The extension of the vector $c$ is essential for taking nondeterministic frictions into account. Besides of that, the sensitivity analysis procedure may have to be adapted as well. Since for each point of support of the discretized optimization problem the single deterministic outcome is replaced by a whole set of outcomes caused by stochastic and/or game-theoretic variations, one may fit a smooth surface middling out the variations. A typical candidate for such a surface is a quadratic multivariate polynom of the form

$$y = d + \sum_i d_i x_i + \sum_{j \leq j} d_{jk} x_j x_k.$$ 

The coefficients of the fitted surface can then be used for deriving the sensitivity coefficients $s_i$ for the parameters $x_i$.

4.4 Assessing Local Variations: Robustness Measure

As stated above, nondeterministic frictions are taken into account by considering the set of possible futures generated by these frictions. At first, we consider the case of stochastic frictions. Due to their local nature, they can be characterized by the size of deviations from the deterministic outcome. Here, this quantity is measured by the robustness of the outcome, since it assesses the stability of the selected action schedule $\mathcal{A}$ with respect to the influence of frictions. A robust schedule $\mathcal{A}$ is a plausibility argument for the feasibility of $\mathcal{A}$.
Robustness has been defined in many different ways [3]. For our purposes, we will define robustness as the degree to which a system can preserve a given set of system properties with a given set $F$ of (stochastic) frictions applied to the system. The term ‘preservation of system properties’ means that the cost estimates provided by the evaluation measures $c_j$ do not exceed excessively the outcome for the friction-free situation. The set $F$ is given by the frictions included in the underlying model as e.g. seen in figure 7. Though $F$ may be limited to stochastic frictions, it may also include other frictions as well.

Formally [35], the robustness $B_j$ of the system $S$ against a set $F$ of frictions can be described as

$$B_j = \int_F D(c_j(y_f)) \cdot L(c_j(y_f)) dy$$

with $y_f := S_f^L (x)$ for an action schedule $A$ and under influence of a friction $f \in F$. The function $L(c_j(y_f))$ gives the likelihood density for an evaluation measure value equal to $c_j(y_f)$. Using the abbreviations $y_f := S_f^L (x)$, $y := S_f (x)$, the assessment function $D(c_j(y_f))$ is defined as follows

$$D(c_j(y_f)) = \begin{cases} 
1 & \text{for } c_j(y_f) \leq c_j(y) \\
0 & \text{for } c_j(y_f) > c_j(y) + \delta \\
c_j(y)/c_j(y_f) & \text{for } c_j(y) < c_j(y_f) \leq c_j(y) + \delta 
\end{cases}$$

Let us take a closer look at the different cases. If $c_j(y_f)$ is less or equal than $c_j(y)$, then the friction (unexpectedly) improves the outcome compared to the friction-free situation. This is considered as perfectly robust, and thus a value of 1 is assigned. On the other hand, if the inclusion of the friction $f$ is worsening the outcome by more than a predefined offset $\delta \geq 0$ compared to the friction-free situation, a value $D(c_j(y_f)) = 0$ indicates the presence of a fundamental problem. For the remaining third case, which describes a situation between these two extremes, the value of $D(c_j(y_f))$ is given by $c_j(y)/c_j(y_f)$. Since the condition of this case is given by $c_j(y) < c_j(y_f) \leq c_j(y) + \delta$, it holds $c_j(y)/c_j(y_f) \in [0,1]$. Due to $0 \leq c_j(y) < c_j(y_f)$, the division is well-defined. Summing up, $D(c_j(y_f))$ returns a relative assessment of the robustness of the outcome by comparing the evaluation under frictions with the corresponding value for the friction-free situation.

The definition of $B_j$ has to be discretized for assuring computability. Accordingly, the codomain $[0,\infty[$ of the components $c_j$ of the evaluation measure is binned by a partition relation $\sim$ to a countable range of values. Based on this modification, the robustness given by the integral (7) is approximated by the sum

$$B = \sum_{Z \in \{c_j(y_f)\}} D(Z) L(Z)$$

Robustness is measuring specific effects of stochastics on the final outcome. A canonical method for calculating the robustness [3] is the execution of $N_B$ Monte-Carlo runs. This means in effect, that for calculating $B_j$ for each of the $m^n$ points of support a total of $N_B \cdot m^n$ simulation runs are necessary. The choice of $N_B$ depends on the required statistical significance, the underlying model of variations as for example stochastic vs. systematic variations, and the structure of the model. This topic is not discussed here any further.
4.5 Frictions causing Global Variations: Risk Measure

Though stochastic variations will usually produce only minor deviations from the expected behavior, large deviations may very well occur with a small probability. Large deviations may also be caused by other players belonging to the system and pursuing own interests. The already known robustness measure $B_j$ provides the fraction of outcomes, which are deviating significantly from the friction-less outcome due to the inclusion of frictions, but it does not provide any statement about the system behavior in the case of a large deviation. The epidemics management specialist may be very well interested in such statements, however, for deciding whether the system behavior in the presence of frictions is either predominantly good-natured or fatal. For closing this gap, the determination of a risk measure is recommended here, which covers the whole space of possible outcomes.

Formally, the risk is defined as expectation value of a loss function over a set of possible hazards for the system. In our case, the loss function is given by an evaluation measure $c_j$ assessing the costs associated with the corresponding outcome of the simulation run. The hazards to be taken into account are the frictions $f \in F$. Thus, the risk is calculated based on the likelihood $L(y_f)$, that a friction $f$ occurring in a situation with an intended action schedule $A$ produces the costs $c_j(y_f)$. This leads to the expression

$$R_j = \int_F c_j(y_f)L(c_j(y_f)) df$$

(9)

As in the case of robustness, we have to assure computability by discretization. This gives

$$R_j = \sum_{Z \in \{c_j(y_f)\}} ZL(Z)$$

(10)

For computing the risk, two quantities have to be provided — likelihood and costs. Concerning the likelihood, one has to ask, which outcomes — distinguished by values of the evaluation measure $[c_j(y_f)]$ — are produced with which frequency. A simple approach for answering this question is to execute several Monte-Carlo runs. Monte Carlo simulations do not always suffice, however. So called LPHC-events (Low-Probability High-Consequence) may be missed by Monte Carlo runs due to their low probability, but may be a significant contribution to the overall risk due to their high criticality. For the handling of LPHC events, special methods have been developed; we will not discuss this topic any further, though, and assume for reasons of simplicity, that the risk is determined by executing a certain number of simulation runs. Thus, instead of a single simulation run for calculating the deterministic evaluation measures $c_j(q)$ a number $N_R$ of such runs is necessary at each point of support analogous to the robustness measure $B_j$. Summing up, this leads to a total number of $N_R \cdot m^n$ simulation runs for determining $R_j$.

5 Outlook: Discussion and Advanced Problems

For providing a realistic model of epidemics management, many complications have to be taken into account. They can be represented in a hybrid model combining system dynamic aspects and the decision-making process of epidemics management. The usage of such a model for the main task of epidemics management — optimizing the epidemics countermeasures — is impeded by its complexity. Notably the stochastic of frictions and their effects contribute to the complexity, because their inclusion in the assessment is realized by extending the
corresponding criteria vector by robustness and risk measures. This extension is acceptable because complexity reduction methods as presented in section 4.2 can be applied in case of need. On the other hand, robustness and risk provide important additional informations about the stochastics.

Robustness can be understood as the ability of an epidemics management policy to tolerate perturbations caused by unforeseen frictions and to maintain its effectiveness. The more robust an epidemics policy, the less probable are necessary adaptations of the policy to changed conditions. Consequently, this property allows the epidemics manager to assess, to what extent the many uncertainties of reality are tolerated. Typically, solutions of an epidemics management problem with large robustness are preferred.

The risk measure takes the criticalities of disadvantageous outcomes (e.g. because of delayed countermeasures due to frictions) weighted by its likelihood into account. Since at least in some cases preemptive countermeasure may avoid or mitigate such disadvantageous developments, risk may be an important tool of epidemics management. Typically, epidemics management policies with a low risk are preferred.

Based on robustness and risk measures, the paper shows that the epidemics management problem with inclusion of frictions is tractable in principle. As was indicated in the introduction, it exists a large number of application domains potentially affecting epidemics management via frictions. This poses some danger to be confronted with the problems of a world model [56] as the one discussed by the Club of Rome [43].

Systems like Forrester’s world model can not include all relevant aspects in appropriate detail. For epidemics management, this means that we will not be able to make valid predictions under all circumstances. Taking the responsibility of humans for decision-making as an example, the complexity of human nature is a principal obstacle for predictability. Forecasts can trigger a change in behaviour, humans can learn and try alternatives in similar situations, some decisions do not follow from facts but are characterized by instability and randomness. Consequently, the accuracy of predictions is not only determined by the quality of the underlying model but by luck as well. An accurate prediction depends on the fortune to guess the decisions made by politicians and other stakeholders and the events occurring in the system. Though the higher complexity of the epidemics management model considered in this paper can not guarantee correct predictions, it increases the chances of a good approximation. It is a tool for calculating what-if scenarios, for providing an impression of the possible futures, and for showing up eventually dangerous developments in the system behavior.

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