Chapter 2
Gene Drives Touching Tipping Points

Broder Breckling and Arnim von Gleich

The Relevance of Tipping Points to Understand Implications of Deliberate Release of Self Propagating Artificial Genetic Elements (SPAGE)

Tipping points and tipping elements, phase transitions and similar critical phenomena are widely discussed in scientific as well as socio-economic contexts as components to understand unforeseen far reaching changes and critical transitions from one stage into another in complex systems caused by small perturbations or gradual changes. For the risk assessment of self-propagating artificial genetic elements in self-sustaining wild populations of animals or plants, it is crucial to understand, where tipping elements could become relevant, how they could be anticipated and to what extent surprises and unexpected effects might occur.

Tipping points are an issue studied in a wide scope of scientific disciplines. According to Lenton (2013) the term tip point "was first introduced in sociology in the 1950s to describe the percentage of nonwhite residents in a US city neighbourhood that would trigger a white flight" (p. 2 with reference to Grodzins 1957). There exists a long scientific tradition of research regarding tipping points in physics (Domb and Green 1972 ff) and a tradition in ecosystems theory and application as well: The concept of tipping points helped to understand severe transitions in system structures (Scheffer et al. 2001; de Yong et al. 2008). Actually tipping points are intensively discussed as a component of 'systemic risks' regarding climate change (Lenton et al. 2008; Lenton 2011a, b, 2012) and turmoil in financial markets (Sornette 2003). By signing the Paris Agreement (United Nations Climate Change 2018)

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an attempt to avoid catastrophic disruptions by touching tipping points in the climate system[1] even found its way into international regulation. It was claimed that limiting the raise of the global average temperature to 2 °C (or better to 1.5 °C) would keep climate change within the normal range of climate variation (cf. Nordhaus 1975; Rijsberman and Swart 1990; Randalls 2010; Lenton 2011b[2]).

Tipping points may be rare,[3] but when they are touched they often lead to catastrophic consequences.[4] Lack of knowledge, surprises, rare extreme events with severe consequences (called 'black swans' Taleb 2007) combine the debate about tipping points with the debate about precaution and the precautionary principle.

Tipping points refer to situations, where exceeding a particular (known—or previously unknown) threshold relates to subsequent and frequently self-amplifying changes over time, which lead to different systems states or even overall changes in the organization of a system. For biological systems, Schwegler (1981) developed a typology (see Fig. 2.1). There are numerous tipping points for which we already know the mechanism (the switch, the tipping element) and the triggered dynamics (bifurcations, phase transitions etc.). Regarding the triggered dynamics there is a wide scale of important differences in magnitudes. When positive feed-back processes are triggered, there might be changes that are difficult or even impossible to reverse, that do not allow recovery. Taleb et al. (2014) call this phenomenon "the risk of ruin" (p. 2f.).

Tipping points refer to critical systems stages, where smallest impulses or gradient shifts can trigger far-reaching consequences. A tipping point delimits domains of different dynamic behaviour of a system. When dealing with tipping points, 1. initial states/dynamics, 2. impulses, 3. tipping elements (structures or functions that can switch in the system, control parameters), 4. tipping mechanisms (swings, transitions, bifurcations, phase changes, etc.) and 5. the new states or dynamics are to be considered. Many of the aspects relevant to anticipate dynamic processes may be incompletely known or even unknown. Though tipping phenomena are part in everyday life and we are familiar with many of them, there are also surprising tipping phenomena with more or less far-reaching consequences. For those with the spatially and temporally highest impact, scientific approaches are required for adequate handling

[1]For instance, a shutdown of the large ocean circulation or a massive permafrost melting.

[2]Lenton however argued that "Yet, no actual large-scale threshold (or 'tipping point') in the climate system (of which there are probably several) has been clearly linked to 2 °C global warming" and he adds additional perturbations as possible triggers of tipping points: "distributions of reflective (sulfate) aerosols, absorbing (black carbon) aerosols, and land use could be more dangerous than changes in globally well-mixed greenhouse gases" (Lenton 2011b, p. 451).

[3]"The traditional deterministic chaos, for which the butterfly effect was named, applies specifically to low dimensional systems with a few variables in a particular regime. High dimensional systems, like the earth, have large numbers of fine scale variables. Thus, it is apparent that not all butterfly wing flaps can cause hurricanes. It is not clear that any one of them can, and, if small perturbations can influence large scale events, it happens only under specific conditions where amplification occurs" (Taleb et al. 2014, p. 12).

[4]"Passing a tipping point … is typically viewed as a 'high-impact low-probability' event" Lenton (2011b, p. 201).

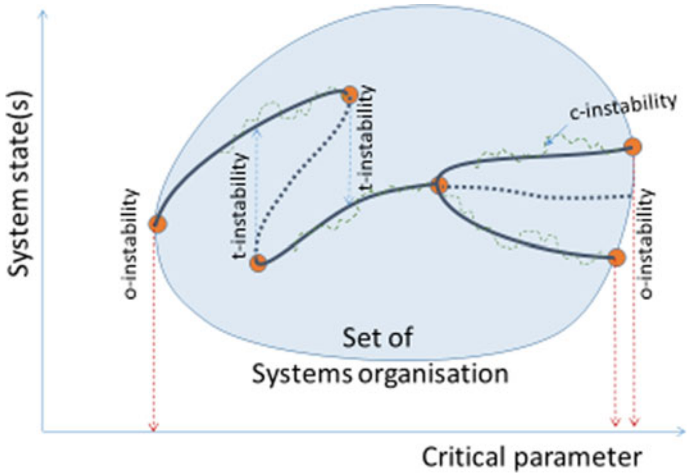

Fig. 2.1 Schwegler (1981) and (1985) introduced a formal stability concept which distinguishes transitions that are to be seen as tipping points (re-drawn and adapted). *c-instability* (named after the climax state of ecosystems) is the domain of system states that can be reached through parameter variations without discontinuities in the system development. This includes the passing of bifurcation points. A *t-instability* occurs, if a transition between segregated branches of stable state occurs as it is the case in hysteresis. *O-instability* means a transition, which is irreversible and leads to a loss of systems organisation

strategies. Along with advances in the theory of complex dynamic systems (homeostasis, self-organisation, emergence, chaos theory, synergetics, operations research), research has increasingly focused on problems of unpredictability, or the attempt to prepare for possible surprises through non-linear behaviour at tipping points. Areas of such precautionary research on tipping points are e.g. medicine, psychology, psychiatry, ecosystem theory, meteorology and research on climate change as well as social sciences and economics, especially business and finance. In this context, a separate research direction has emerged that deals with the precautionary question of the extent to which a threatening approach to a tipping point with serious consequences can be detected in good time for possible countermeasures (early warnings). Our work on possible tipping points in connection with research and development, regulation and release of gene drives can be classified here. We are primarily concerned with tipping points in technology development (technology characterisation), in the (agricultural) ecosystems that can be expected to be affected (vulnerability analysis) and in the areas of technology governance and acceptance/acceptability. The focus is on 'reasons for high concern' that can justify precautionary measures.

Perturbations touching tipping points may trigger completely unexpected behaviour of the system, confronting us with surprises. Such surprises are known from dealing with (socio-) ecological (Holling 1978; Filbee-Dexter et al. 2017), socio-economical (Kim and Mauborgne 2003; Helbing 2012) and socio-technical systems (Taleb 2007). Thus the interest of research on tipping points not only lies in the identification and description of different characteristics of tipping points but more and more in precautionary research about the possibilities and limitations to timely identify indications, that a system is approaching a tipping point. There is a growing literature about 'early-warning signals for critical transitions' in complex dynamical systems (Scheffer et al. 2009; Lenton 2011a). Its focus lies on system dynamics and tipping elements. Important aspects of tipping elements are thresholds, bifurcations and basins of attraction. If these elements and their consequences are already known and can be analysed empirically, scientific approaches are possible based on statistics (probabilistic forecasting) and on dynamic modelling (see Table 1 in Lenton 2011a). Identified as generic 'early warning signals' are certain courses of system behaviour like increasing time for recovering from perturbations, increasing autocorrelation, increasing variance, increasing skewness and flickering (ibid., see also de Yong et al. 2008; Veraart et al. 2012; Andersen et al. 2009; Carpenter et al. 2011 and regarding financial markets Wanfeng et al. 2010 and Gatfaoui and de Peretti 2019).

Still more challenging is the identification of tipping elements of which the consequences are still unknown because they did not yet happen or should not happen at all. A possible approach is the analysis of the dynamics and the structure (architecture) of the system. Regarding system dynamics, the above mentioned early warning signals of system behaviour may be helpful to identify even not yet known bifurcations or basins of attraction. It is an aim of the modelling efforts as described in Chap. 5 to contribute to such an approach. Regarding system architecture, a structural vulnerability analysis taking into account results of research on 'resilient systems' should be helpful (see Chap. 3: "Analysis of Vulnerability of Ecological Systems"). Taleb et al. for instance identified 'the connectivity of a system' as a potential for the 'propagation of harm' and they add that our socio-technological and socio-economic global systems are extremely interconnected especially by transportation and information technology ('the global connectivity of civilization', Taleb et al. (2014, p. 4)). For them 'invasive species' and 'rapid global transmission of diseases' are among the severest historical consequences. They recommend "boundaries, barriers and separations that inhibit propagation of shocks" (p. 10). The character of interconnections within systems is indeed an important aspect of vulnerability or resilience, others are structural and functional diversity and redundancy, buffers and stocks that increase resilience or the lack of which may trigger bifurcations or phase transitions (von Gleich and Giese 2019).

The capability of triggering bifurcations, phase transitions, alternative dynamic regimes or alternative stable states is not limited to the state and structure of the affected system. It is as well depending on the character and magnitude of the perturbations. And regarding gene drives we are dealing with self-amplifying perturbations. We focus on ambitions to develop organisms with a modification that facilitates gene drives. A gene drive is a genomic construct which enables a higher rate of inheritance of the construct than those occurring naturally as a result of Mendelian inheritance (Burt 2003). The character and magnitude of perturbation caused by gene drives is dependent on the one side on the implemented functionality, which can be very powerful and on the other hand on the extremely extended exposure (see Chap. 1

Technology Characterisation). Self-propagating exposure magnifies the opportunities to touch otherwise unreachable tipping points and thus increases the probability of the occurrence of 'black swans', of extremely improbable, "unforeseen and unforeseeable events of extreme consequences" (Taleb et al. 2014, p. 1). This is the reason why Taleb et al. (2014) request "more precaution about newly implemented techniques, or larger size of exposures" (Taleb et al. 2014 p. 7). Regarding tipping points, the expectable impact of technological interventions into socio-ecological systems can be identified by the method of a structural vulnerability analysis, with its focus on weak points independent of certain perturbations (see Chap. 3: "Analysis of Vulnerability of Ecological Systems"). An important element should be the test of model processes. Whenever an apparent trend to a significant alteration in a given context occurs, it is reasonable to ask in which way tipping point dynamics could be involved in order to understand ongoing and coming developments.

We already mentioned that tipping points occurred and may occur in socio-technological systems. With regard to molecular biotechnological developments we are apparently in an accelerated innovation phase, where rapid transitions occur, where new and previously inaccessible technical options are on the way to become feasible. The construction and especially the release of Self-Propagating Artificial Genetic Elements (SPAGE) in wild living populations of organisms is in itself touching a tipping point because of the new quality of technical power and the intended self-propagating exposure.

To outline how the understanding of the involvement of tipping points contributes to a rational understanding of the ongoing developments, we first discuss the significance of tipping point dynamics in exemplary contexts well established in the scientific discourse. Therefore, we summarize frequently used formal types of tipping points known from the analysis of dynamic systems. Then we take a look in which regard the concept of tipping points helps to understand the potential transitions that are involved in possible applications of SPAGE. For this purpose, we use a systems hierarchy approach to address the different organisation levels which could be influenced by tipping point transitions.

Conceptual Background: Phase Transitions in Dynamic Systems

We first take a look at examples of phase transitions in different scientific contexts. This underlines that tipping point dynamics are not a singular phenomenon in ecology but a fundamental topic in science dealing with dynamic systems, for which a considerable body of theory is available that helps to understand possible risks and supports the development of adequate handling strategies in various contexts. With regard to tipping points it became obvious that they are of specific importance in the management of ecological systems and that concept transfers between different disciplines helped in understanding case-specific details.

Examples in Different Scientific Domains

Phase transitions that take place when exceeding critical stages in various physical, ecological and even socio-economic contexts encompass scales from the global level down to small-scale systems. We summarize some of the most widely studied systems where tipping points are crucial for understanding.

Biosphere Ecology: Global Climate Change

As already mentioned tipping points are mainly discussed in the current scientific as well as public debate with regard to the global climate system and the changes that global transitions may bring for regional scales, land use, and security of coastal zones (Bindoff et al. 2014; Parmesan and Yohe 2003; Harley et al. 2006). It is assumed, that the global climate system represents a steady state with limited random shifts close to an equilibrium which depends on the overlay of different feedback mechanisms. Disturbances which might raise the global average temperature above about two degrees is currently assumed to activate processes that lead to further warming and potential unmanageable transitions in the global climate system (Lenton 2011b). These processes are referred to as tipping elements in the global climate system (Lenton et al. 2008). Considerable efforts in research as well as in political administration on various levels are on the way to identify and to quantify these potentially critical thresholds and avoid the exceedance of tipping points beyond which undesirable self-amplifying traits gain an extent and intensity that might go beyond available management capacities and lead to an overall state of the global climate system which provides less management options than the currently prevailing state of the global climate system.

There are several critical components considered, which may be involved in the tipping point dynamics within global climate system (Fig. 2.2): A particular extent of global warming could reduce polar and high mountain ice cover. This would significantly reduce the earth's albedo, i.e. the light reflection of the earth and the absorption of solar irradiance would increase. This could lead to further melting of ice leading to further warming until a higher equilibrium would be reached (Notz 2009; Lenton 2012). Another tipping element could be the thawing of permafrost soils, driving the system in the same direction. The onset of bacterial activity in water saturated and previously frozen soil with a high content of dead organic material would lead to the release of large amounts of CO_2 as well as methane (CH_4) to the atmosphere. Methane is about 34 times higher in efficiency as a greenhouse gas than CO_2 (Dean 2018; Biskaborn et al. 2019). Another tipping element could be the release of methane hydrates in the ocean shelf marginal areas, which might become unstable when water temperatures increase (Kvenvolden 1988; United Nations Climate Change 2014). Global climate research attempts quantifications of these and additional other tipping elements as well as counteracting processes to come up with

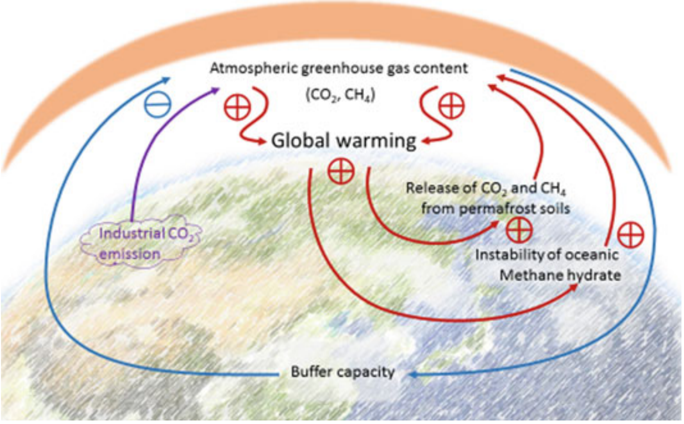

Fig. 2.2 The global climate is governed by a variety of interlinked feedback processes, among of which are the release of carbon dioxide (CO_2) and methane (CH_4) from thawing permafrost soils, and methane release from potentially instable methane hydrates under sediments on the ocean floor as a result of increasing temperatures. In the discussion on global warming, it is considered as probable, that tipping points exist, beyond which there would be the onset of a self-amplifying shift towards a different equilibrium of globally higher temperatures. Though a global trend is generally widely detected, there is uncertainty remaining how the different processes are interlinked and how a new equilibrium would stabilise

an integrative picture in which tipping point dynamics appear to play a crucial role for the understanding of long-term and large-scale dynamics.

Tipping point dynamics have a crucial role also in many smaller scale processes.

Fire Ecology

In many ecosystems, fire is an important structuring factor. In landscapes where accumulated organic matter is sufficiently abundant and dry, fire events of various orders of magnitude can take place as a regular part of the systems dynamics. Fire ignition can have natural reasons (e.g. lightning, electrostatic discharges) or emerge due to anthropogenic influence. The attempt to understand the rapid transition process from heat mediated, self-amplifying transition of organic material to ashes led to the development of a specific scientific discipline: fire ecology—with an elaborated body of empirical as well as theoretical findings (e.g. Goldammer 2012). This encompasses the insight, that large-scale natural fire are a regular component of those landscapes, in which a pronounced seasonal change between draught and humidity facilitates an accumulation of organic material. Fire events become the more probable to expand, the higher the amount of accumulated combustible material is. In these landscapes, fire leads to a characteristic vegetation pattern with larger even-aged plant stands, which result from the temporal synchrony of re-growth starting

(Johnson 1996). Young vegetation usually has a reduced inflammability which is successively increasing with age. An interesting implication is, that an anthropogenic suppression of the fire outbreak without reducing combustible material (e.g. through prescribed fires) might increase the risk and the extent of large fires and thus the subsequent damage potential of single events (Piñol et al. 2005). The critical point that triggers the phase transition in fire ecology is apparently the randomly occurring igniting event. How far the single event expands across larger parts of the landscape is influenced by the particular vegetation structure and the extent of available combustible material which was accumulated in the ecological system (Chandler et al. 1983).

Fire ecology can also be used as an example to explain that the tipping point concept is helpful on different levels of the same context: Landscape analysis can bring about insight in a further tipping element. In random pattern of inflammable and non-inflammable sites a density threshold can exist beyond which the spatial range of a fire tremendously expands (see the explanation below under percolation).

Population Ecology: Outbreaks and Epidemics

The population outbreak dynamics that can be observed in some biota, e.g. in the form of plankton blooms appears to be phenomenologically related. There are modelling approaches departing from similar formal descriptions. In aquatic systems there is the possibility of a sudden extreme quantitative increase of particular species with dramatic consequences for other organic ecosystem components. While usually being embedded in stabilizing nutrient capacity limitations or predator–prey interactions, an escape from these limitations can occur under certain conditions and give rise to extremely increasing, several orders of magnitude higher population densities (Hallegraeff 1993). In these systems, a precise tipping point is not easy to determine, though in dynamic model representations the behaviour can be studied (e.g. Huppert et al. 2002).

The outbreak of epidemics and biological invasions follows comparable patterns and is frequently analysed with similar formal approaches (Earn et al. 2000).

Aquatic Ecology: Alternative Stable States in Shallow Lakes and Other Ecological Systems

During the 1970s it was discovered, that in temperate climates shallow lakes can shift between two different types of organisms that dominate the species composition (biocenosis). Under otherwise comparable external conditions, the biocenosis can be either dominated by ground-rooted macrophytes or alternatively by plankton algae. After extensive limnological studies (Scheffer et al. 1993; Scheffer and van Nes 2007) the conclusion was drawn, that it is possible to force transitions between these different states. Such a transition can be induced by considerably increasing or decreasing the nutrient load, in particular phosphate: A strong eutrophication allows the plankton to thrive to an extent that the macrophytes are shaded out and vanish from the system. The other way round, a restoration of the macrophyte dominance requires an extensive removal of nutrients—far more than required to establish the algae-dominated stage. It occurs, when the nutrient limitation is sufficiently pronounced so that algae density becomes sufficiently thin so that shading of macrophyte re-growth is no more efficient.

This type of switching between alternative stable states is known also from a variety of other, in particular physical, systems (e.g. magnetism, Jiles and Atherton 1986). The involved direction-dependent transitions are called hysteresis (Mayergoyz 2012 see also Fig. 2.9). In an ecological context, the shallow lakes were one of the first examples in ecology being studied and successfully modelled on a quantitative basis. Meanwhile, this example encouraged additional research for comparable phenomena in other ecosystems. Today, quite a number of other ecological processes is known that follow an according pattern. Scheffer et al. (2001) provide a list of studies describing this type of ecological transitions.

Concepts and Applications in Dynamic Theory: Important Forms of Phase Transitions Where Tipping Points Mark Domain Boundaries

The previously described examples have been modelled in formal structures which can be assigned to specific forms of transitions. While the global climate system requires an overlay of a number of different counteracting processes of different dynamic forms, the conceptual understanding of other transition processes is less complex and it is easier to identify a limited number of dominating drivers. Knowing them informs about the repertoire of approaches that could play a role also with regard to SPAGE. The following dynamic paradigms are frequently employed to understand tipping point dynamics. A number of approaches was developed for mathematical modelling of physical and chemical as well as for ecological and social systems, which capture different tipping point situations. The approaches illustrate, that the metaphor of a tipping point summarises different forms, applicable to particular situations.

Balance and Seesaw

The most simplistic form of a tipping point model follows the idea of a balance or a seesaw (Fig. 2.3). Putting increasing amounts of weight on the lighter side leads to an equilibrium point on which both sides reach equivalence. Exceeding this point causes the system to flip over. A fundamental characteristic of tipping points is apparent in such a system: For a distinction to which side the seesaw will tilt, there are large domains where changes in load have a limited effect. This is different precisely at

Fig. 2.3 An infinitely small impact can be linked to an infinitely large effect. This is characteristic for a seesaw precisely at the tipping point

the tipping point. At the tipping point, infinitesimal influences can be decisive, to which side the seesaw tilts. Prigogine and Stengers (1984) argue for a generalization of the effect: that at the tipping point, the principle of causality, i.e. the consistent connection of quantifiable cause and effect, does not hold, because for this point no finite relation of cause and effect can be specified. Precisely at the border between two different dynamic domains infinitesimally small influences can trigger effects of any order or magnitude—depending on the systems specification. With regard to SPAGE, it can be argued, that resulting parameter changes can influence ecological balances and shift systems states towards new equilibria. Models (see Chap. 5) can illustrate such an effect.

Domino Effects: Iteration

Spatially extended iterative processes are a significant domain for tipping point dynamic studies. The domino effect (Fig. 2.4) can be seen as a simplistic model of such an iterative phenomenon. In systems, where long cause-effect chains play a role, small-scale local events can affect their neighbourhoods in a way that the

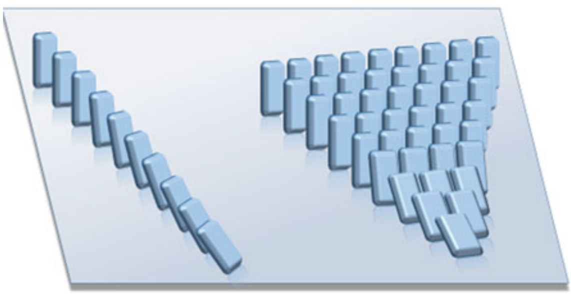

Fig. 2.4 Falling domino pieces are a frequently used metaphor and abstraction of interlinked cause-effect chains. In an ecological context, it has to be emphasised, that this kind of chain- or network-propagation is not necessarily linear but can in principle also follow amplification dynamics including exponential processes

change in a local state is transmitted to the surroundings. If the latter is capable to perform the same transition, large-scale macroscopic results can be caused by a local tip. A chain, where the fall of a single domino stone causes the next one to fall demonstrates a linearly proceeding dynamic. It is equally possible that an array is exposed in a way that one stone interacts with two or more others. Then specific exponential processes can emerge.

With some extensions, critical mass dynamics can be described by such an approach: The atoms of some radioactive elements decay at a random rate and emit particles and/or radiation. If they hit other kernels in the surrounding, they can induce additional fissions from which more particles are emitted. In a sub-critical mass, the spontaneous decay induces on average less that one additional fission in the surrounding. If, however, the density of unstable atoms within the energetic range of emitted particles is sufficiently high, an exponential increase of radioactive decays would emerge as a chain reaction and cause a nuclear explosion. The critical mass is specified by the probabilistic condition that on average, the fission of a single atom must cause more than one additional fission event (Holdren and Bunn 2002).

It is obvious to identify for such a case a tipping point with the critical mass. Other models of cascading effects follow comparable dynamics. This is in particular the case for outbreak and epidemic processes which occur in population systems. Its relevance for the SPAGE context results from its importance for inter-generational self-amplification.

Excitable Media

A variety of chemical reactions (e.g. Belousov–Zhabotinsky reaction, Briggs–Rauscher reaction) as well as physiological (e.g. neuron excitation, tachycardia and ventricular fibrillation) and ecological systems reaction (e.g. some lichen growth forms and vegetation pattern) can be described by the excitable media type of interaction. It is one of the basic forms of a pattern-generating mechanism in spatially structured self-organising systems. In these spatially structured systems, three different states can occur locally: 1—a locally *excitable* state which can persist for long times until it is activated by 2—an *excited* state occurring in direct neighbourhood. Then 1 also transits to the excited state. In analogy to a chain reaction thus the excitement can spatially propagate. The excited state persists for a particular time span and then turns into 3—a *refractory* state, which is no more excitable for a specific time span required for a regeneration of the excitable state. The local transitions are usually modelled on a grid to study the emergence of spatial patterns (Fig. 2.5). Though the underlying conception is rather simplistic, an according parametrization approach facilitates possibilities to describe a wide variety of pattern generating processes. A large body of literature exists, theoretical studies (Holden et al. 2013; Meron 1992) as well as applied studies (Kapral and Showalter 2012; Mosekilde and Mouritsen 2012). Fire ecology can be considered as a special case of an excitable media system, where the excited phase is comparatively very short, and the refractory phase by far longer. Also many processes of invasions or epidemics and a number of predator prey

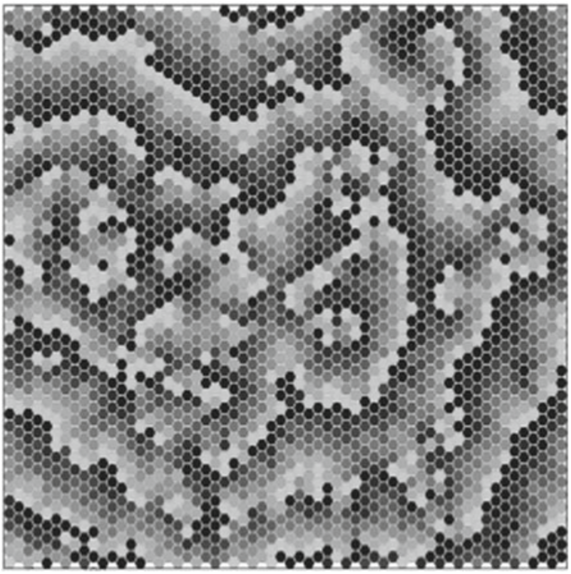

Fig. 2.5 Excitable media pattern:
The spatially distributed alteration of a locally excitable, excited and refractory state (equally: susceptible, infected, recovering) is used to describe a wide variety of biological as well as social pattern generating processes. Among typical spatial pattern that can occur, are coherent spiral waves as well as transient random configurations. Here, a simulation on a hexagonal grid is shown where the transition from an excited to an excitable cell occurs at a probability of 0.5, while remaining for 3 iterations in an excited, and 4 iterations in a refractory state before returning to excitable. The grayscale indicates the age of the cells after the most recent excitation with white as the most recently excited and black as excitable. The simulation started from a random distribution of 54 excited cells on a 30 x 90 grid

interactions can be captured and studied in this form (Breckling et al. 2011; Makeev and Semendyaeva 2017). In these models, the transition from excitable to excited can be interpreted as a tipping event, furthermore there are parameter specifications beyond which the observable pattern transits to different characteristics. Because of its relation to ecological dispersal processes, the approach can help to understand dynamic phenomena of SPAGE dispersal the same way as conventional ecological dynamic can be modelled.

In epidemics, the according states frequently are named "susceptible, infected, recovered" and are modelled in random networks (Volz and Meyers 2007). For SPAGE the model type is of interest because it provides a way to describe long-term and large scale dispersal effects basing on a specification of strictly local interactions.

Percolation

With regard to ecological application potential, percolation theory is to some extent related to excitable media. A grid-based process is considered in which permeable and impermeable cells are randomly dispersed. In such a setting, it is statistically analysed, at which density of randomly dispersed permeable cells a continuous connection of opposite sides of the grid becomes probable (Fig. 2.6). As soon as a grid type specific density (the percolation threshold) is exceeded, percolation takes place with a high probability, otherwise not. It is remarkable that the threshold stands for a rather sharply dividing boundary which can be considered as a specific form of a tipping point. Percolation theory has various applications in physics as well as in epidemiology and ecology (see e.g. Boswell et al. 1998; Davis et al. 2008). To fire ecology, percolation theory contributed the following interesting result. In a random landscape consisting of flammable and non-flammable spatial components (local sites), fires rapidly extinguish when the overall frequency of randomly distributed highly flammable locations is below the percolation threshold. Above the percolation threshold, however, there is a high probability that local fires expand throughout the entire landscape (in a model: across the grid). At the percolation threshold itself (the tipping point), there is a singularity: the way the fire has to take across the landscape would be the longest compared to other constellations, and the intensity in terms of synchronously burning sites would be the lowest possible above extinction (Galeano Sancho 2015). In such a situation, the fire (or otherwise represented dispersal process) would persist for the longest temporal range directly before percolation would occur. For ecological applications, percolation analysis can help to decide, whether a population could sustain with regard to the particular biogeographical setting, which is an important question in an assessment of gene drive persistence.

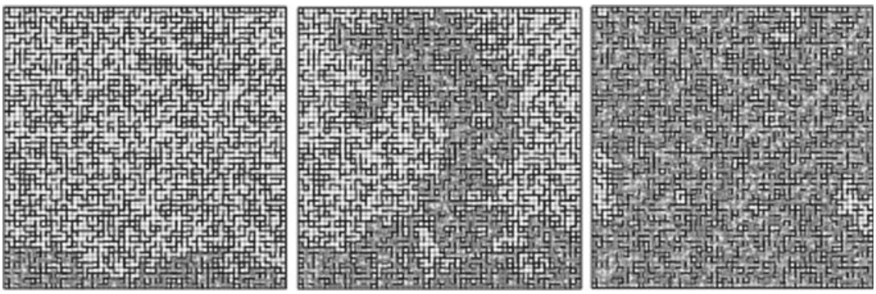

Fig. 2.6 Percolation models are used to describe dispersal processes in heterogeneous media. When an increasing rate of randomly placed local obstacles are placed across a grid, a characteristic tipping point emerges above which for almost any configuration a transition throughout the grid is possible. Three configurations are shown, one below (left), one above (right) and one close to the percolation threshold (middle). The system at the tipping point has specific characteristics. Percolation models are used e.g. in physics, in soil science but also in landscape ecology to analyse dispersal and persistence pattern of organisms in fragmented environments. For gene drive organisms the approach is highly relevant to assess overall implications of altered abilities to cope with local spatial resistance

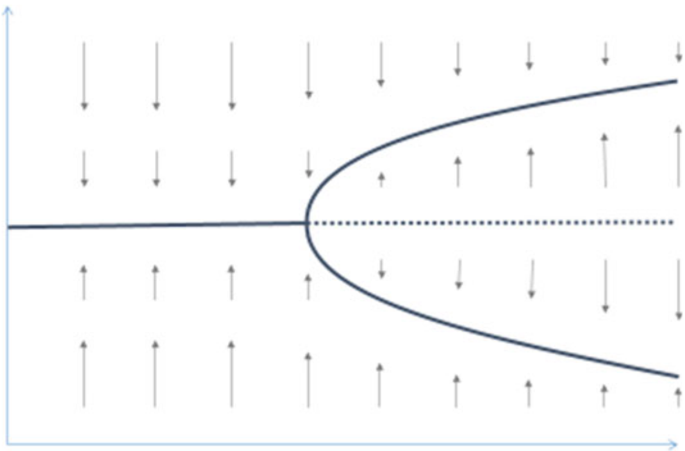

Fig. 2.7 Bifurcations occur in dynamic systems as a result of a non-linearity. A typical example is the pitchfork bifurcation. The normal form of the according differential equation is $dx/dt = r * x - x^3$. When increasing the critical parameter r, a tipping point occurs beyond which the configuration transits from a globally stable state to a configuration with two alternative stable states separated by an unstable equilibrium (dotted line). In many physical systems as well as in ecological population dynamics this type of tipping point can be observed

Threshold Effects and Phase Transitions, Bifurcations and Hopf-Bifurcation

It is a major issue in dynamic theory to analyse forms of transitions which can occur in systems in which causal structures determine the change of states over time. A typical transition occurring at a tipping point is a pitchfork bifurcation (Fig. 2.7). If a system reaches a critical state, at the bifurcation point an infinitesimally small influence can decide, to which side of a "pitchfork", that characterizes possible stable states, the system will develop. Also for this scenario, the characterisation by Prigogine and Stengers (1984) is applicable that at the bifurcation point there is an exception in an otherwise coherent causal structure.

A bifurcation named after the Austrian mathematician E.F.F. Hopf is a transition where the stable state of a system becomes unstable and a limit cycle occurs when a critical threshold (bifurcation point or tipping point) is exceeded (Fig. 2.8). A variety of oscillatory processes in ecology can be described with a Hopf bifurcation model (e.g. Fussmann et al. 2000).

Hysteresis

For the discussion of tipping points in the given context, hysteresis is one of the significant forms of transition and plays a central role in the climate change debate. Hysteresis is a system structure with a domain in the state space where alternative

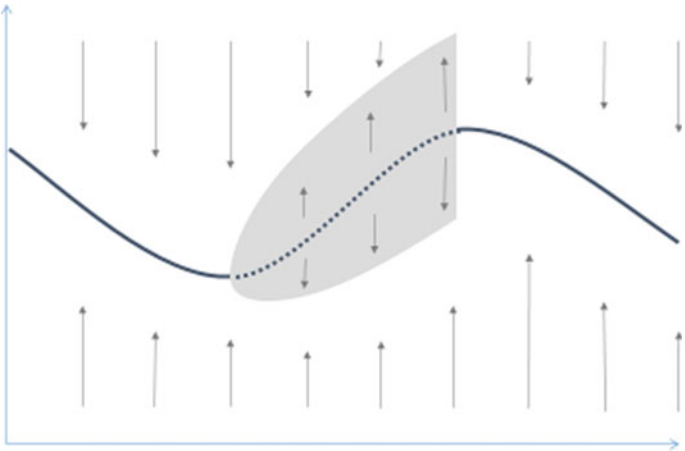

Fig. 2.8 Hopf-bifurcations occur also in population dynamics: Beyond a tipping point, a stable equilibrium becomes unstable and a limit cycle occurs. This is a transition from a stationary stable state to a stable periodic oscillation. Grey area: Domain of a critical parameter where oscillatory behaviour occurs

stable states are possible, i.e. under exactly the same external conditions the system will remain in either one of two possible states. This implies that the system description goes beyond a plain functional relationship where each input is related to only one specific output. The parameter domain in which alternative stable states occur, is usually limited. The hysteresis effect occurs, when the limiting parameter is exceeded and the system flips into the other one of two states. As a characteristic property, the transition from stable state 1 to stable state 2 happens at a different size of the critical parameter than the return from stable state 2 to stable state 1. The description of such a transition requires a three-dimensional representation (Fig. 2.9). Conceptual descriptions are given e.g. by Scheffer et al. (2001) and Gordon et al. (2008). The analysis of relations in an ecological context as well as with regard to the global climate system have brought about a large number of illustrative cases (Scheffer and van Nes 2007). For SPAGE the approach is of high interest since it provides an explanation, under which conditions a system could shift to a basically different set of states, which can be very difficult to restore and get back to previous states.

After having discussed a short survey of examples and formal constructs in which the effect of critical conditions and tipping points are captured, we now analyse potential occurrences of tipping points with regard to the new genomic constructs like SPAGE and gene drives. There are indications that some of the major forms in which tipping points occur, are highly likely to play a significant role also for an understanding of implications of a deliberate release of SPAGE.

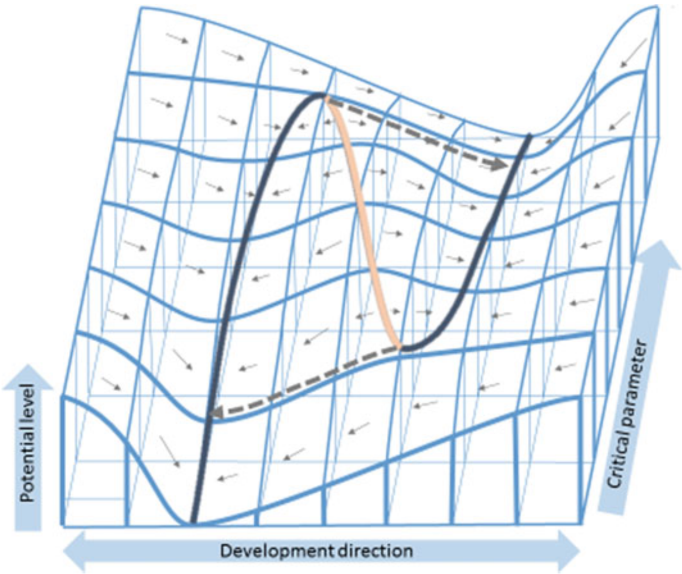

Fig. 2.9 Hysteresis can occur in an ecological context where the change of a critical parameter leads to an abrupt transition towards a new equilibrium (bold dotted arrows). There is the specific condition that the reversal occurs at a different value of the critical parameter. This comes with the implication of the existence of two alternative equilibria for a particular size range of the critical parameter. This behaviour is known for a variety of ecological systems, including shallow lakes in temperate climate. For global climate change a related configuration is also in discussion

Potential Tipping Points with SPAGE Involvement

When considering SPAGE, tipping points can be discussed on various levels. Though at first glance it may seem likely to think of molecular properties of the transgenes in first place. However, since the implications of SPAGE are necessarily embedded in a wider ecological and social context, the possibility of tipping point dynamics must be also expected in a wider spectrum of contexts. *A systematic assessment is an open and important research question, which requires substantial attention and an effort in interdisciplinary exchange.* Here, we can provide an outline and first hypotheses on tipping point dynamics and associated model forms.

A Hierarchy in Consideration Levels: Where SPAGE-Related Tipping Points Could Occur

In ecology, the assignment of interactions to specific levels of organization was established as an efficient approach for structuring and systematisation. How to do that is summed up under the term hierarchy theory (O'Neill et al. 1986). Organisation levels

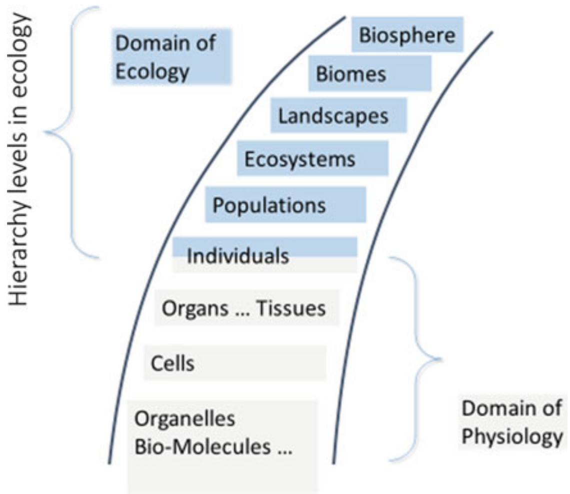

Fig. 2.10 Hierarchy theory is used to structure the topics dealt with in biology. Levels are distinguished according to emergent properties. From lower to higher levels, additional interaction types play a role which require specific forms of descriptions and which are not relevant on the lower levels. The physiological domain consists of biomolecules, cell organelles up to the level of the individual. From individual to the biosphere we have the ecological domain. To study each of the levels, requires specialised expertise

are distinguished according to specific properties that emerge on a particular level as a result of systems internal interaction and self-organisation (Fig. 2.10). In ecology, mainly the levels *organism—population—landscape—biome* and *biosphere* are distinguished. The approach is complemented with an extended view including additional levels from the molecular level up to the largest known macroscopic structures to facilitate interdisciplinary connections and views (Jantsch 1980).

Tipping Points on the Molecular and Physiological Level

The very first tipping point, proof of concept and SPAGE feasibility, can be considered as being passed. This was a transition from largely conceptual considerations (Burt 2003) to finally successful efforts on the molecular level to produce and implement an artificial genomic structure which is inherited to subsequent generations at higher rates than the natural Mendelian inheritance. From the very beginning, such a structure can be combined with other and in the end potential harmful properties on the population level (Hammond et al. 2016).

For gene drives, a next critical threshold would be a release, which means that alterations on the molecular level that lead to a manifestation on the individual level would become connected to higher levels of naturally self-organising systems, i.e. the population level and communities of organisms (ecosystems). This threshold requires, that a considerable body of regulation, risk assessment and public discourse would have to be developed and settled beforehand. This is currently not the case. Relevant questions to manage the risks, uncertainties and lack of knowledge which are created by the release of gene drive organisms are not solved—but the according scoping has been started (Oye et al. 2014). In the meantime, laboratory development under controlled conditions continues towards a differentiation and diversification of the approaches, as we described in the Chaps. 1 and 7.

Tipping Points on the Population Level

On the population level, a variety of different SPAGE constructs and species specific tipping points have to be considered. For a prospective analysis of the dynamic behaviour of SPAGE organisms detailed modelling studies would be required. The modelling set-up would have to encompass studies of individual interactions as well as large-scale spatially explicit (meta-) population representations, comparable to and expanding the modelling approaches (as laid out in Chap. 5). Phase transitions that occur when transgressing tipping points on this level can be structural shifts of systems on local, regional or potentially even global range, including extinction events. Various dynamic regime shifts, trophic network alterations including secondary higher trophic level effects, virulence changes, etc. have to be assessed. Depending on the type of SPAGE, transitions like bifurcations, limit cycles, strange attractors and hysteresis can be phenomena on this level. It has to be emphasised, that regardless of the efficiency of population level model projections, long-term predictions concerning the evolutionary fate of a specific release are likely to remain in the domain of the "unknown unknowns" (see Chaps. 1 and 9).

Tipping Points on the Ecosystem Level

The ecosystem level encompasses the overall budgets of energy and matter transformation jointly brought about by the community of organisms on the basis of the available bio-element reserves and energy basis including inputs into and outputs from the system (Jax 2016; Breckling and Koehler 2016). It is the integrating level at a specific site with sufficiently reasonable internal structural homogeneity. Comprehensive ecosystem studies are difficult, complex and therefore rare. Frequently, ecosystem investigations focus on specific ecosystem-related aspects like ecosystem services (Fischlin et al. 2007) or ecosystem integrity (Woodley et al. 1993). Both approaches are of a high importance for the impact assessment of SPAGE technologies.

Concerning systemic tipping points, an ecosystem assessment would in particular focus on key processes and key species. Ecosystem engineers (Jones et al. 1994) are species, which provide through their activity structures and conditions that largely influence the overall systems characteristics and composition of the overall community. Keystone species (Paine 1966) have a central function in the structuring of the trophic relations and thus the overall systems condition, frequently through indirect effects. If species with such a pronounced role in the ecosystem would be directly or indirectly affected through population alterations caused by a SPAGE, this might have consequences where tipping point dynamics on the ecosystem level may become apparent. An implication is, that through matter-, energy- and information-processing on the ecosystems level, minor impacts can be damped, amplified or transformed. Anticipation of these effects is notoriously difficult, but therefore not irrelevant. Knowledge in this field was accumulated in particular in conservation ecology (Schwartz et al. 2000) and in restoration ecology (Jordan et al. 1990).

Tipping Points on the Landscape and (Cross-) Regional Level

The landscape level encompasses a network of different ecosystem types (Forman 2014). Here, the spatial aspect of process organization is in the foreground. Spatially explicit approaches like grid-based models, an ecological version of cellular automata (Breckling et al. 2011) are used on this level e.g. with relation to excitable media or percolation. Furthermore, individual-based models (Łomnicki 1999; Judson 1994) with their high level-integrating potential are used to analyse the role of organism's activities across larger spatial scales in heterogeneous structures (see Chap. 5). Well known tipping points on the landscape level result from fragmentation effects (Opdam et al. 1993), and are an issue analysed in metapopulation theory (Hanski 1999) and population viability analysis (Beissinger and McCullough 2002) as far as referring to large-scale structures.

Tipping Points in an Evolutionary Context

The evolutionary context of SPAGE is probably the aspect that involves the highest degree of relevance from a perspective of risk analysis, since it deals with long-term implication on a scale and temporal extent which goes beyond direct empirical accessibility. Unfortunately, it is also the domain that allows the least precise prediction and maintains in scientific processes the highest level of irreducible uncertainty and "unknown unknowns". This is because the evolutionary process connects small-scale processes on the molecular scale, i.e. mutations, with macroscopic selection processes on the level of the whole organism through the amplification of fitness-related reproduction dynamics further on with large-scale landscape and community relations. Key issues for an understanding of evolutionary processes are considerations of a multi-level selection which acknowledge, that evolutionary change is not exclusively an interaction between genome and a particular environmentally determined fitness trait but that fitness consists of a variety of components which can be distributed and interfere across different levels. The other decisive theorem comes under the name of the "red queen hypothesis" (Van Valen 1973). This widely discussed hypothesis puts forward that fitness is neither an intrinsic property of an organism nor stationary. Instead, it is a continuously changing relation of the members of a population and their environment, which is influenced from both sides. This requires—in order to maintain a currently held position—an ongoing change. Thus, even for a stationary state, an underlying evolutionary adaptation would be required.

For evolutionary dynamics, models usually can make qualitative and probabilistic statements, which may outline expectations. Models also can give clear indication, that it is highly unlikely to predict the potential fate of a SPAGE in an evolutionary perspective. Reliable quantitative predictions in this domain can be assumed to be rare. On a meta-level we can discuss the conclusion whether tipping points of SPAGE in an evolutionary domain indicate an irreversible phase shift from known unknowns to unknown unknowns.

Tipping Point Considerations with Regard to a Social Ecological Domain of SPAGE—The Interaction of Natural and Social Processes

Systems descriptions, though mainly used in scientific processes, have been applied to describe changes and transitions in social and economic dynamics (Becker and Breckling 2011). Therefore, it is a reasonable question to study, how the availability of SPAGE may influence ongoing processes in a social ecological context (Becker and Jahn 2006) and what kind of tipping points might occur in this context. Since it is apparent, that SPAGE open up new opportunities as well as new and potentially risky and controversial developments (Oye et al. 2014; Esvelt et al. 2014), it is a useful and necessary task to identify qualitative transitions in the use of the technologies and employ the concept of tipping points to analyse and understand transitions concerning e.g. land use, health, economy, regulation, public involvement, and issues how the feedback between socio-economic activities and ecological development is operated. In the following we list a number of starting points for investigations aiming at an identification of such SPAGE related tipping points in the social ecological domain.

Tipping Points in Application and Feasibility Considerations

A first basic transition following a balance (or seesaw) paradigm was apparently passed already and this opens the space for transitions in succeeding domains. The prospects of gene drives were postulated from theoretical grounds (Burt 2003), however, their realisation turned out to be difficult if not unfeasible with means available at that time. CRISPR/Cas was originally not developed for the production of gene drives (Jinek et al. 2012). Evolved in bacteria, its natural function is to defend a bacterial cell against viral intrusion. Once CRISPR/Cas was isolated, characterized, and its mode of action understood, it became apparent that it enables various additional uses. It turned out that it could be applied also as an instrument enabling the steps which are necessary to manage the molecular obstacles in the construction and implementation of gene drives. This transition from conceptual reasoning to practical availability enabled various kind of gene drive applications (e.g. Buchman et al. (2018) for the fruit fly *Drosophila suzukii*, Gantz et al. (2015) for the mosquito *Anopheles stephensi*). What was demonstrated to be feasible now could possibly lead to further frontier crossing, requiring a discourse in additional fields like risk assessment and risk management.

Tipping Points in Risk Assessment and Management

In order to understand risks which are combined with further reaching technologies it is necessary to execute test applications under limited and controlled conditions before first applications. These experiments are set-up to study a given context so that cause-effect networks can be analysed. From an epistemological perspective, this implies specific conditions: A strict delimitation of the experiment from an unobserved surrounding, and a setting that allows to observe or detect relevant intended and potentially also unintended effects. The spatio-temporal extent of these experiments depends on the type of interaction to be studied. Extrapolation from smaller to larger scales are possible as long as re-scaling is reasonable without the interference of processes that lead to changes of the results, i.e. that hierarchy effects, phase transitions or tipping points play a role. Scaling issues are a critical point in risk assessment (Woodbury 2003). A typical example is the discussion about an adequate (and clearly limited) contribution of bio-based energy to the transition towards renewable energy (e.g. Vogt 2016). The larger the spatio-temporal extent, the more difficult and costly experimentation will become. It is apparent and generally accepted in the scientific community, that experiments that regarding their effects cannot be controlled and spatio-temporally limited are irresponsible. This implies, that there is a tipping point up to which sufficient knowledge can be gained and accountability for action can be assigned. A situation, where an experiment would be required for risk assessment that in practice could not be reversed, would represent in the terminology of Schwegler (1981) an organizational instability. In such an experiment the domain of a system's operability is left (see Fig. 2.1). A determination where such a tipping point might occur in the context of deliberation of a gene drive becomes apparent when it would be necessary to practically release a gene drive organism in order to identify implied risks. It is clear, that under controlled conditions not all parameter can be studied that play a role in the wild. In particular spreading, colonization and metapopulation dynamics are difficult to be studied because scaling effects play an important role. This makes it difficult to extrapolate results from spatio-temporally limited conditions.

Tipping Points in Regulation and Law Enforcement

Regulation and enforcement are not to be understood as a process in the same line. In particular, the entry into force of a particular law or a regulation can be considered as a tipping point, which concludes a developmental process. It is quite obvious, that regulation is not a process that follows from scientific advancement or social consensus in a direct and conclusive way. It is a complex interaction that involves social functioning and integration at large. Scientific contributions are part of the input, in addition considerations of the overall legal integrity, ethical considerations and higher level jurisdictional aspects significantly contribute.

For gene drives, it is already apparent from what we know to date, that not all questions that arise in this context are covered by existing regulations. While there are regulations to safeguard laboratory processes (in Germany issued by ZKBS 2016), there are many open questions how to facilitate a secure handling of the emerging hazard and exposure potentials beyond the lab. One of the very obvious issues which requires updated regulation is the expectable conflict with the Cartagena Protocol on Biosafety (Secretariat of the Convention on Biological Diversity 2000). As an international convention, the protocol regulates that the transboundary movement of genetically modified organisms is legal only after an informed consent of the country into which the organism is moved. This was meant to apply for organisms under controlled conditions or under cultivation. For gene drive organisms, it would be required to establish an international consent if species like olive flies, mosquitos or fruit flies would be released, even if the release would initially target only a local population. This is because the construct has a very high probability to become dispersed to other regions. A more detailed assessment of legal implications certainly would identify further open questions. The expanded technological options make it necessary to develop new and more specific and adequate regulations (see Chaps. 8 and 9).

It can be expected, that these new regulations also would require a stricter management of access to the required laboratory material to prevent abuse, as Oye et al. (2014) cautiously indicated. The requirements of an adequate handling of the technological power is currently under discussion rather than being coherently regulated (National Research Council 2015; National Academies of Sciences, Engineering, and Medicine 2016). The transition may take place between a regulatory regime that allows a trans-regional alteration of wild living species characteristics based on individual resp. partial interests or an integrated, international regulatory regime, which would, in order to be efficient, require new enforcement instruments. Most likely, a qualitative transition in trans-boundary regulation would be required to cope with the risks that can be involved by the release of self-propagating artificial genetic elements.

Tipping Points in Social Acceptance

Gene drives, as a type of SPAGE which are designed for efficient dispersal throughout natural populations, are a qualitatively new instrument in nature management. While established methods of genetic modification were justified by promises like bigger harvests and to be indispensable to feed the world with regard to the limited planetary resources, gene drive technologies promise, among others, a relief of major human diseases through elimination of vectors, elimination of significant agricultural pests, breaking of pesticide resistance developments, and elimination of invasive species (Collins 2018). Since for some of these promises, at least a technical feasibility seems credible, it requires a profound technical, ecological as well as ethical discourse.

With the experience of the debate on genetically modified crops in Europe during the last two decades it is apparent, that there seem to be tipping points also in discourse dynamics. In other upcoming technical domains risk assessment and its public perception, proponents and opponents were engaged in a constructive exchange of arguments; for the introduction of nano-materials see e.g. Filser (2019) and Wigger et al. (2015). In contrast, for the GM debate it turned out, that apparently there are at least bi-stable results possible. On the one hand arguments are used selectively as instruments to follow pre-defined business intentions rather than being primarily problem-oriented. On the other hand, unsatisfiable requests for zero risk were raised. For the discourse on SPAGE it will be an interesting research domain, to assess, how ethical considerations, scientific progress in SPAGE development, the perception of the economic potential and political influences merge either to shape public consensus or to fuel an 'us versus them' attitude. Promises, disappointment, credibility, and willingness to trust will play a significant and to-date not foreseeable role.

Discourse Outlook

SPAGE are a topic, which gains significance the more application attempts beyond laboratory conditions are proposed. The release of self-propagating artificial genetic elements which are intended to operate beyond the capability to control, withdraw or limit their proliferation in any way poses new questions. Incorporated in self-reproducing organismal entities, which are subject of evolutionary changes, of combination and interaction with an untested and untestable manifold of self-amplifying contexts, potential SPAGE application apparently requires answers to the question how to delimit domains of acceptability, how to discuss, draw and enforce lines that would be unjustifiable to be crossed. *These are typical thresholds characterized by tipping points.*

To minimise the probability that un-ethical results derive from "good intentions", it seems of high priority to debate this issue not only within the scientific community. It is required to involve not only molecular scientific expertise but also landscape ecological, geographic and ethical expertise, among others. It would be of equally high significance to facilitate a general public discourse that brings the topic to the attention of the broader public in a way that is not primarily driven by feasibility, fascination or scandalisation but sheds light to problems of knowability as well as reversibility and control.

We need to be aware that a release of SPAGE affects several tipping points. The technological power and range of SPAGE result in a range of effect potentials that cannot be holistically assessed in its implications for the biosphere. May be for the first time, humans are acquiring the potential to use the self-organisation potentials of populations to drive artificial properties into natural population including detrimental ones which have the potential to induce extinctions. It is by far not the tipping point that this would enable human induced extinctions of wild living populations for the first time. But that extinctions could be enabled by molecular tools and be lab-made and releasable is so fundamentally new, that regardless of specific application intentions, the handling of this potential requires extensive public insight, control and regulation, considerations and the highest achievable standard in ethical argumentation.

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