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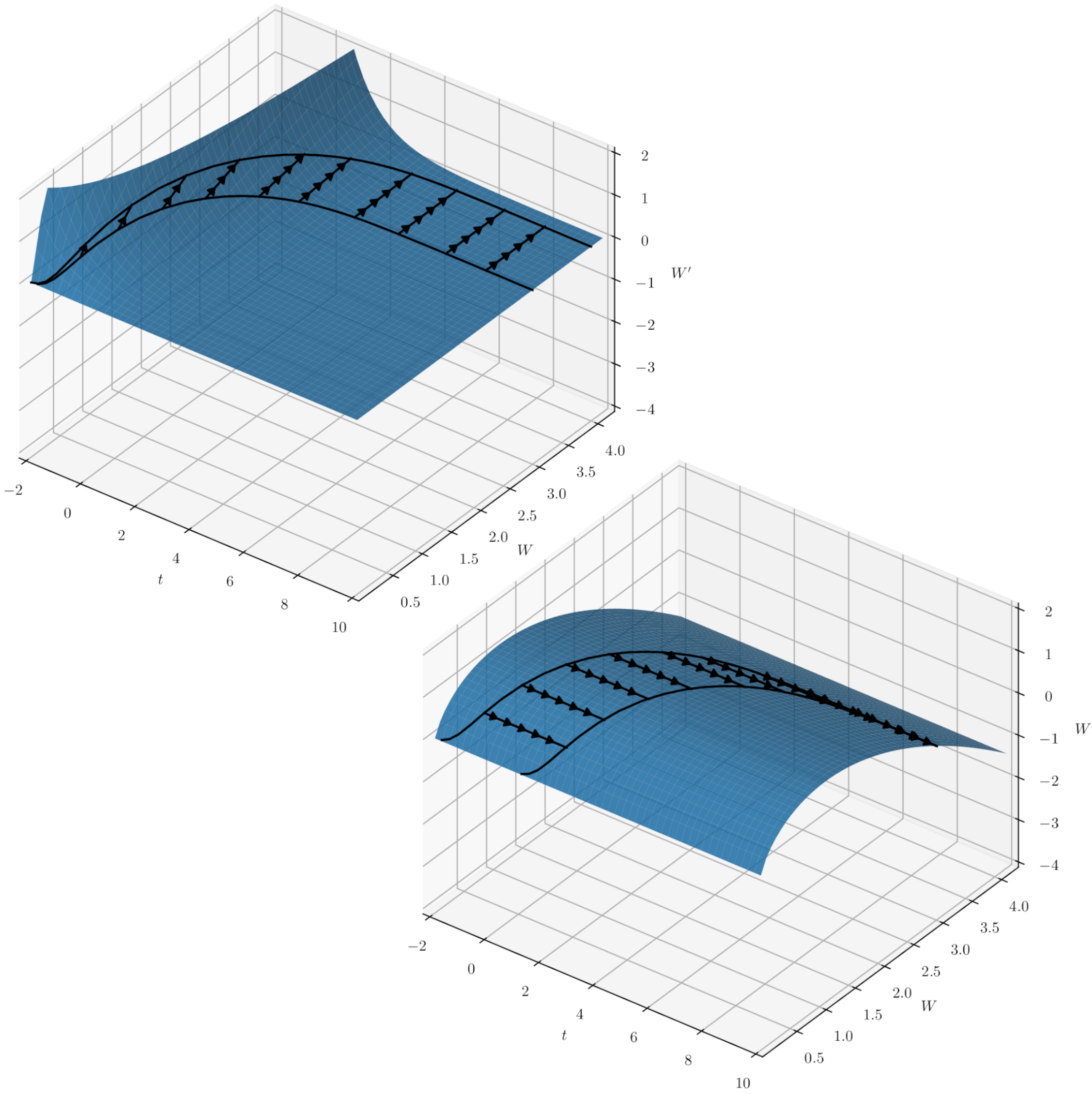

Symmetries of Mathematical Models in Biology

Master’s thesis in Engineering Mathematics and Computational Science

FELIX AUGUSTSSON

DEPARTMENT OF MATHEMATICAL SCIENCES

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Cover: The jet surfaces of the classical and autonomous Gompertz models, with representative transformations of respective Lie point symmetries, acting on a common solution curve of the two model formulations. Generated with Matplotlib in Python, with code availible at the repository described in appendix A.

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Abstract

In biology, a common type of mathematical model is systems of first order ordinary differential equations (ODE:s). In general, large non-linear systems of ODE:s have no analytic solutions. Mathematical symmetries can however still be used to analytically study differential equations, without the need to find explicit solutions. Symmetries are transformations that map solutions of a differential equation to other solutions, and thus contain a lot of information about the system. However, due to the historical development of the theory of symmetries alongside physics, the literature on finding symmetries of the type of large systems of first order ODE:s usually found in biology is sparse.

In this thesis, four biological models using first order ODE:s are studied using Lie point symmetries: the Hill equation, the Gompertz model, the Lotka–Volterra predator–prey model and the Yildirim–Mackey lactose operon model. Symmetries of all models are found using ansätze. Additionally, symmetries are found using a repurposed method based on parameter independence. It is also shown that, using both methods for finding symmetries, sophisticated computer algorithms are needed for the calculation of symmetries of bigger systems to be viable.

Additionally, the general structure of symmetries is investigated for different formulations of the Gompertz model. It is shown that the two scalar Gompertz model formulations found in literature are symmetrically special cases of the original system formulation, and the consequence for model building in biological systems is discussed.

It is concluded that due to the generality of the mathematical theory, symmetries show promise of being a useful tool when studying mathematical models in biology. However, several mathematical problems have to be solved before symmetries can be used in day–to–day biological modeling.

Keywords: Lie symmetries, Lie point symmetries, First order ODE:s, Gompertz model, Lotka–Volterra predator–prey model, Yildirim–Mackey lactose operon model, Lie algebra

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I would also like to thank the other members of Cvijovic Lab. Having weekly check-ins with you has created something akin to a normal work environment during this time. It has made all the difference.

Furthermore, I would like to thank Olle Lexell. Our lunches have been a needed distraction from my work, even when they, as they often did, devolved into mathematical discussions.

Lastly, I would like to thank Emelie Sjögren. Your patience and positivity have helped me when things got too overwhelming. I do not think everything would have gone as well as it did without you.

Felix Augustsson, Gothenburg, June 2021

Je n'ai fait celle-ci plus longue que parce que je n'ai pas eu le loisir de la faire plus courte.

Blaise Pascal

Contents

Introduction

In many scientific fields the concept of symmetry is important. Symmetries bridge the gap between the qualitative and the quantitative; it is both a statement about what a system is, and how a system can be measured. In most cases when symmetries are discussed, the symmetries in question are simple, geometric symmetries. These can be mirror symmetries, as that of a face, or rotational symmetries, as that of a dice. But from a mathematical point of view, the concept of symmetries is far broader.

This more general view of symmetries is used in physics to describe the fundamental properties of the universe. These properties are called conservation laws, and are one of the many tools that have given physics its stable theoretical basis. Establishing an equally solid theoretical framework for other fields, such as biochemistry and ecology, is of great interest. In these fields the systems studied are of great complexity, just as in physics, but the design of experiments poses other challenges to those whishing to study them. Since the studied subjects are often alive, distinct phenomena can not be entirely isolated when designing experiments. While great progress has been made in the fields, the question still stands: which properties are inherent of these living systems, and which properties simply emerge in the modeling of the systems?

Symmetries could be one of the keys to answering this question. However, the mathematics involved when studying these types of symmetries are involved, especially when applying them to systems unlike those found in physics, around which much of the mathematics has evolved. This thesis therefore tries to chart some ground when it comes to applications of these methods to specific models. Several models, stemming from both biochemistry and ecology, are studied. The models vary in complexity, which allows the strength of the techniques to be displayed for simpler models, while still highlighting the obstacles of applying the methods to the complex models used at the edge of current research.

The common denominator for the models investigated in this thesis is that they are based on first order ordinary differential equations (ODE:s). ODE:s are the most common type of models in biology [1, 2], and first order ODE:s in particular are the norm. These models are mathematically distinct from the higher order partial differential equation (PDE) models used in physics. This means that the use of symmetries in the domain of biology is not merely a superficial question of applying known methods to problems from new fields. Instead, even just the initial problem of finding symmetries brings up mathematical questions that are often disregarded in the literature, as first order models are viewed primarily as as a theoretical stepping stone to the higher order models that are traditionally studied.

This thesis focuses on the problem of finding symmetries of mathematical models in biology based on first order ODE:s. Current literature on the computational aspects of symmetries of first order ODE:s is sparse, and mainly aims at finding a particular amount of symmetries [3, 4]. This is due both to there always being an infinite amount of symmetries for first order ODE:s, and due to the intended use of the found symmetries. While one purpose of finding symmetries is to fundamentally understand the studied systems by for example finding conservation laws, another common purpose is integrating problems that are hard to solve. For first order ODE:s, the purpose in the literature almost always falls in the latter category while our interest lies in the former. The focus of this thesis thus centers on finding all symmetries of a first order system given some restriction, so that biological properties can be systematically studied.

Further this thesis aims at framing questions of importance to more widespread adoption of similar techniques in biological fields. These involve both biologically interpreting symmetries, and understanding what the symmetries can be used for. The discussion centers around the studied models, using them as examples to get a better grasp of larger questions. A special focus is put on the Gompertz model, the simplest of the models not previously studied using symmetries.

In chapter 1, a general overview of the use of first order ODE:s as models in biology is given. The four models studied in this thesis are also introduced: the Hill equation, the Gompertz model, the Lotka-Volterra predator–prey model and the Yildirim–Mackey lactose operon model.

In chapter 2, the mathematical theory of Lie point symmetries is introduced. The text is aimed at being accessible to readers who have no prior experience of mathematical symmetries. The first three sections presents and explains the tools necessary for finding Lie point symmetries of systems of first order ODE:s. The sections should act as sufficient background to understand the calculations performed in chapter 3 and 4, given that the reader has a prior understanding of the fundamentals of ODE:s. The last section concerns the underlying algebraic structure of Lie point symmetries. It is significantly more mathematically involved than previous sections out of necessity, and a reader inexperienced in abstract algebra might want to put off reading this section until after chapter 3 and 4.

In chapter 3, symmetries are calculated for the four models presented in chapter 1 using the standard method for first order ODE:s: ansätze. The chapter mostly consists of traditional symmetry calculations, and can thus safely be skimmed if the reader is already familiar with Lie point symmetries.

Chapter 4 contains calculations of symmetries for the latter three models using a method novel in this setting. The method is based on parameter independence, and is repurposed from the subfield of group classification. The method of parameter independence is more systematic than using ansätze, and thus offers a distinct alternative approach to finding symmetries of systems of first order ODE:s.

In chapter 5, different ways of interpreting and using symmetries are discussed in brief. Two such uses are explored further: invariants and the general structure of symmetries. In particular, different formulations of the Gompertz model are compared by looking at the general structure of their respective symmetries.

The thesis ends on a discussion in chapter 6, where the results of are reviewed and put into a more general context. The discussion is aimed at being as non-mathematical as possible, so that readers with any mathematical background can get a feeling for the role symmetries could play in mathematical modeling in biology.

Chapter 1

Modeling in biology

In biology, ordinary differential equations (ODE:s) are a common tool for modeling systems mathematically. The systems are modeled to contain several interacting species, and observable states of the different species. The states vary from field to field, but common types are the concentration of a chemical species in biochemistry, the volume of organs or growths in medical science and the size of populations of certain animal species in ecology. The interaction of the different species is modeled over time, and thus differential equations are a suitable tool. The restriction to ODE:s is often due to the fact that the models required to describe biological phenomena are complex enough, without taking spatiality into account, to be at the boundaries of what is viable to simulate and compare to experiments. There is therefore a large amount of models in these fields that take the form

$$\begin{aligned} \frac{dA^1}{dt} &= \omega^1(t, A^1, \ldots, A^s; \boldsymbol{\theta}) \\ &\vdots \\ \frac{dA^s}{dt} &= \omega^s(t, A^1, \ldots, A^s; \boldsymbol{\theta}), \end{aligned}$$

where $A^1(t), \ldots, A^s(t)$ are the states at time t, and $\boldsymbol{\theta} = (\theta^1, \ldots, \theta^m)$ are a collection of parameters. The parameters allow the models to be adopted to a vast variety of circumstances. They can be related to environmental factors, inherent properties of the species involved or a measurement of a species assumed to be constant for the duration of the experiment.

One major obstacle in modeling and predicting the behavior of biological systems is the ability to correctly estimate these parameters. The reliance on estimated values in models is not unique to biology in the natural sciences, but unlike most other natural sciences the models in many biological fields are constructed based on these types of experiments. While one can in physics isolate different parts of a larger system, and part by part build a theoretical model that is then tested on larger systems, the same approach can not be used in biology as the systems studied are large and intertwined enough that isolation of phenomena becomes nigh on impossible. Instead chemical principles, research on simpler but similar lifeforms and biological intuition is used to build models, which can then be tested against data from living test subjects (in vitro or in vivo). Not only does this affect the speed at which good models can be constructed; it also means that the parameters values that can not be directly measured can not be estimated before any simulation of the model is run, since there is no underlying fundamental model to predict the values with.

To solve these problems, a number of advanced methods have been developed with such sophistication that entirely new fields, such as systems biology, have developed around them [5, 6]. Still, many problems and challenges remain. In this thesis, mathematical symmetries are explored as a possible tool to solve some of these challenges. In order to tackle such a broad question as "Can symmetries be used to enhance biological modeling?", several concrete models from biology have been selected as examples. These examples serve both as a familiar setting for those working in biological modeling to learn about symmetries of differential equations, and as a way to concretely discuss the uses of these symmetries as modeling tools.

The models have been selected to cover a range of biological disciplines, and to cover model complexity ranging from models simple enough to solve by hand to those used in current research. In this chapter the models will be introduced, along with some biological context where necessary.

1.1 The Hill equation

The Hill equation is a scalar ODE that was originally used to model the binding of oxygen to hemoglobin [7]. Since then, it has been used to describe many binding phenomena such as ligand–receptor and substrate-enzyme reactions [8]. It takes the form

$$\frac{dY}{dt} = -v_{\max}\frac{Y^n}{K_m + Y^n} = \Omega_n(t, Y), \quad n > 0, \tag{1.1}$$

where Y is the concentration of the substrate that binds to the enzyme. The parameter $v_{\max}$ models the maximum reaction speed, K_m is a dissociation constant and n is the Hill coefficient. The biological interpretation of the Hill coefficient n has historically been a contentious matter, but it is roughly a measure of the cooperativity among binding sites. The Hill equation has been studied using symmetries of differential equations, using its nondimensionalized form [9]. By nondimensionalizing both the substrate concentration with

$$y = \frac{Y}{{K_m}^{1/n}}$$

and the time with

$$\tau = v_{\max}\frac{t}{{K_m}^{1/n}},$$

eq. (1.1) simplifies to its nondimensionalized form

$$\frac{dy}{d\tau} = -\frac{y^n}{1 + y^n} = \omega_n(\tau, y), \quad n > 0 \tag{1.2}$$

which will be studied in this thesis.

1.2 The Gompertz model

In several fields in- and outside of the life sciences, growth in general plays an important role. In particular, when measuring different phenomena ranging from cell growth to the growth of cities, the concept of exponential growth often appears. Exponential growth stems from a species growing with a rate that is proportional to its size. Written in mathematical terms:

$$\frac{dW}{dt} = cW(t), \tag{1.3}$$

where $W(t)$ is the size of the species (volume of a tumor, weight of an animal, individuals in a population etc.) at time t and c is a constant. While exponential growth accurately models the initial stages of the growth process for many systems, eventually some external factor will limit the growth. The external factor might be simple, like limited availability of food in the case of an animal population, or complex, like limitations of infrastructure in the case of cities. Correctly modeling the external limitations is crucial when studying the long term behavior of the system.

The Gompertz model is one such model that has seen success in many areas. It was first proposed in 1825 as a means of predicting the mortality rate of populations in order to accurately prize life insurances and annuities [10]. Gompertz formulated his model as the differential equation

$$\frac{dL}{dx} = -aq^{x}L(x) \tag{1.4}$$

where $L(x)$ is the number of people living at age x. It is worth noting that for small values of x and $c = -a$, the ODE (1.4) behaves like eq. (1.3). In retrospect this similarity is not surprising as Gompertz modeled the decay of a population, which can be seen as "negative growth". However, this connection was not made at first.

Around a hundred years after the conception of the model, it saw its first use as a growth model in the modeling of economic growth [11, 12]. It was first mentioned in the life sciences in 1926 as a suggestion for an alternative growth model [13], and a few years later saw its first concrete use modeling the weight of cattle [14]. In the century since, the Gompertz model has been used to model the size of a wide range of animals (for a good summary, see [15]). The breadth of animals (and parts of animals) where the Gompertz model can be fitted well to growth data has made this one of the life sciences where the model is most used. The other branch of the life sciences where the Gompertz model has seen success is in modeling tumor growth. The model was first used (apart from as a tool for making graphs [16]) for this purpose in 1964 [17]. It has since become one of the most widely used models for tumor growth [18] (for a summary of applications, see the introduction of [19]). When studying both organism and tumor growth, the same question has been asked about the Gompertz model, namely what the biological interpretation of the model is. In this chapter, this question will be tackled using the theory of Lie point symmetries.

1.2.1 Finding a standardized ODE description

Even though Gompertz first stated his model as the ODE (1.4), the differential form is not the most commonly used. Instead the Gompertz model is usually formulated as the solution to the ODE (1.4). In Gompertz' original paper [10], this function takes the form

$$L(x) = dg^{q^x} \tag{1.5}$$

where $g = \exp(-a/\ln(q))$ in the ODE (1.4). Note that the parameter d is not included in the differential equation but instead stems from the constant of integration. By replacing Gompertz' $L(x)$ (number of people of age x) with $W(t)$ (the size of a species at time t) the function can be used to model growth without any structural changes to the function. The function form of the model is not only sufficient as description when the goal is to fit the model to some data; the third parameter d is necessary since it relates to the initial value needed to solve the ODE (1.4). However, as will be seen in the next chapter, eq. (1.5) is not a form where the type of symmetries used in this thesis can be employed. Additionally, the function is not parametrized consistently across literature, varying depending on field and taste. To analyze the model with Lie point symmetries it is therefore necessary to determine two things. Firstly it must be established what is meant by "The Gompertz model" when viewing the model as an ODE through a life since lens. Secondly, a standardized and meaningful parametrization of the model in ODE form must be established in order to gain insight from the later symmetry treatment.

Since the function form of the model is sufficient and necessary to match the model to data, the ODE form is only found in the literature as a means of providing a background to the model. The ODE formulation thus often lacks proper references, rendering the origin of the formulation hard to trace. All formulations of the ODE found in the literature can however be sorted into one of three families.

The ODE:s in the first family can all be written on the form

$$\frac{dW}{dt} = re^{-bt}W(t). \tag{1.6}$$

These ODE:s are reparametrizations of Gompertz' original ODE (1.4), often emphasizing the expected behaviors of the model in the growth context by choosing parameters that should be positive. In the parametrization seen in the ODE (1.6), r should be positive for the species size $W(t)$ to grow (as opposed to shrinking or decaying) and b should be positive for the growth to reduce over time (and thus limiting the growth). Solutions to this family of ODE:s can be seen in fig. 1.1.

The first family of ODE:s is tightly related to the second family, which can be written on the form

$$\begin{aligned} \frac{dW}{dt} &= G(t)W(t) \\ \frac{dG}{dt} &= -bG(t). \end{aligned} \tag{1.7}$$

This system of ODE:s could also be argued to be the original Gompertz ODE, since the original differential equation (1.4) was motivated by Gompertz in the following way:

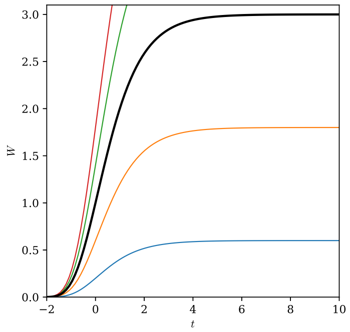

Figure 1.1: Example solutions curves of the classical Gompertz model with varying initial values for W.

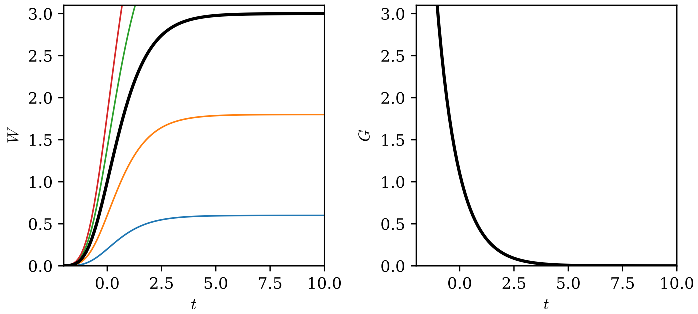

Figure 1.2: Example solutions curves of the system Gompertz model with varying initial values for W.

> If the average exhaustions of a man's power to avoid death were such that at the end of equal infinitely small intervals of time, he lost equal portions of his remaining power to oppose destruction which he had at the commencement of those intervals, then at the age his power to avoid death, or the intensity of his mortality might be denoted by aq^x, a and q being constant quantities; ([10, p. 518])

The intensity of mortality can be seen as $\gamma(t)$ in the ODE (1.7), with $\gamma(t) = aq^x$ serving as a solution to the lower equation in the ODE (1.7) when $\ln(q) = -b$. Solutions to this family of ODE:s can be seen in figs. 1.2 and 1.3. Since the ODE (1.6) is a partial solution to the ODE (1.7), the formulations that can be written on the form of the former equation will henceforth be referred to as "classical Gompertz ODE:s", while the latter formulation will be referred to as "classical Gompertz ODE:s on system form" or simply "system Gompertz ODE:s". The classical Gompertz ODE is the form used in the first paper on biological growth [14].

The third family of ODE:s appear slightly later in the literature. They can all be

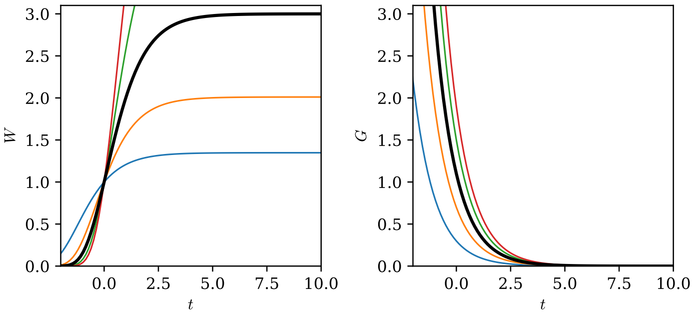

Figure 1.3: Example solutions curves of the system Gompertz model with varying initial values for G.

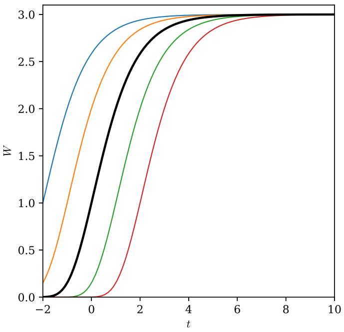

Figure 1.4: Example solutions curves of the autonomous Gompertz model with varying initial values for W.

written on the form

$$\frac{dW}{dt} = -\alpha \ln\left(\frac{W(t)}{K}\right) W(t). \tag{1.8}$$

While solutions to this ODE are all Gompertz curves, it is important to note that this formulation is fundamentally different than the classical ODE (1.6). This is clear from the fact that while the ODE (1.6) is directly dependent on time, the ODE (1.8) is not. We will therefore henceforth refer to the family of ODE:s that can be rewritten as the ODE (1.8) as "autonomous Gompertz ODE:s". Solutions to the autonomous Gompertz model can be seen in fig. 1.4. The first time an autonomous Gompertz ODE appears in the literature on biological growth is in a review of the new use of the Gompertz curve in 1932 [20]. In the review (which also features a classical Gompertz ODE) the autonomous form is used to liken the Gompertz curve to another popular growth curve, the logistic growth curve, in order to generalize the Gompertz model.

In order to better understand what separates the classical and autonomous ODE:s, a consistent parametrization is required. Due to the sporadic use of the ODE form, no such standardization has been made. The function form, on the other hand, has seen efforts of standardized parametrization. [15] (concerned mainly with the growth of organisms) shows that most parametrizations found in the literature belong to two parametrization groups. Both parametrizations groups have in common that they have two shape parameters and one location parameter, where this third parameter only controls how far the curve is shifted in the time direction. In both groups the shape parameters serve the same purpose, but the location parameter can serve two distinct useful purposes, resulting in the two forms of parametrization: the T_i- and W_0-forms [15]. These two forms can be canonically parametrized by

$$W(t) = Ae^{-e^{-k_G(t-T_i)}} \tag{1.9}$$

and

$$W(t) = A\left(\frac{W_0}{A}\right)^{-e^{-k_G t}} \tag{1.10}$$

respectively. These two parametrizations are useful, since the parameters A, k_G, T_i and W_0 have clear interpretations. A is the value of the upper asymptote, also known as the carrying capacity of the system. k_G, although lacking in interpretation itself, is proportional to $k_U = k_G/e$, where k_U is the relative (to A) maximum slope during the process. Together, A and k_G control the shape of the curve. T_i or W_0 depending on the formulation control the localization of the curve. T_i is the point in time where the curve achieves its maximum slope, also known as the point of inflection. W_0 on the other hand is the size at $t = 0$. Depending on application either of these two parametrizations might be useful. It is therefore necessary to reparametrize both the ODE (1.6) and the ODE (1.8) using both forms.

To reparametrize the ODE:s using Gompertz curve parametrizations, the solutions of the ODE:s must be found. The classical Gompertz ODE:s (1.6) and (1.7) are most easily solved using the fact that the classical ODE is separable to integrate over W and t separately. The solutions are thus

$$W(t) = ce^{-r/b \cdot e^{-bt}} \tag{1.11}$$

where c is an arbitrary constant. The autonomous Gompertz ODE (1.8) is most easily solved using the variable substitution $y(t) = \ln(W(t)/K)$ where the resulting ODE is readily solved. The solutions are thus on the form

$$W(t) = Ke^{ce^{-\alpha t}} \tag{1.12}$$

where c is an integration constant. Comparing the solutions in eqs. (1.11) and (1.12) to the T_i- and W_0-formulations in eqs. (1.9) and (1.10), the relationships

$$\begin{aligned}
b &= k_G \\
r &= k_G e^{k_G T_i} \\
r &= k_G \ln\left(\frac{W_0}{A}\right) \\
\alpha &= k_G \\
K &= A
\end{aligned}$$

between the parameters can be found. The classical Gompertz ODE:s (1.6) and (1.7) and the autonomous Gompertz ODE (1.8) can thus be reparametrized as

$$\text{Classical,}\qquad T_i :\qquad \frac{dW}{dt} = k_G e^{-k_G(t-T_i)} W(t) \tag{1.13}$$

$$\text{Classical,}\qquad W_0 :\qquad \frac{dW}{dt} = k_G \ln\left(\frac{W_0}{A}\right) e^{-k_G t} W(t) \tag{1.14}$$

$$\text{Autonomous,}\quad T_i \text{ and } W_0 :\qquad \frac{dW}{dt} = -k_G \ln\left(\frac{W(t)}{A}\right) W(t) \tag{1.15}$$

$$\text{System,}\quad T_i \text{ and } W_0 :\qquad \begin{aligned} \frac{dW}{dt} &= G(t)W(t) && \text{(1.16a)} \\ \frac{dG}{dt} &= -k_G G(t). && \text{(1.16b)} \end{aligned}$$

There are two important notes worth highlighting: Firstly, all of the classical and autonomous formulations have a two-dimensional parameter space (even eq. (1.14) since W_0 and A only appear in the composite form W_0/A). This must be the case since only a two parameter ODE can produce three parameter solutions (which the Gompertz curves are). Secondly, it should be stressed that eqs. (1.13) and (1.14) are just two different parametrizations of the same differential equation. They will thus share symmetries, and calculations need only be performed on one form.

1.3 The Lotka–Volterra predator–prey model

A classic model for predator-prey dynamics is the Lotka–Volterra model, modeling two populations where one species feed on the other according to

$$\begin{aligned} \frac{dN}{dt} &= aN - bNP && \text{(1.17a)} \\ \frac{dP}{dt} &= cNP - dP, && \text{(1.17b)} \end{aligned}$$

where N is the prey population size and P the predator population size [21, 22]. The parameter a is the rate at which the prey population grows without interference, b and c how the predator and prey populations affect each other and d the rate at which predators die without prey to hunt. Solutions to eqs. (1.17) can be seen in figs. 1.5 and 1.6. The Lotka–Volterra model is by no means the most modern or correct model to use in most situations, but the model is important from a historical perspective [23]. Variations of the model have been analyzed using symmetries [24, 25], but there is a lack of interpretations of the symmetries in such literature as well as studies of the original model.

1.4 The Yildirim–Mackey lactose operon model

A more modern model in the style and scope of those used today in biology is the Yildirim–Mackey model for the Lactose Operon [26]. It models the biochemical reaction

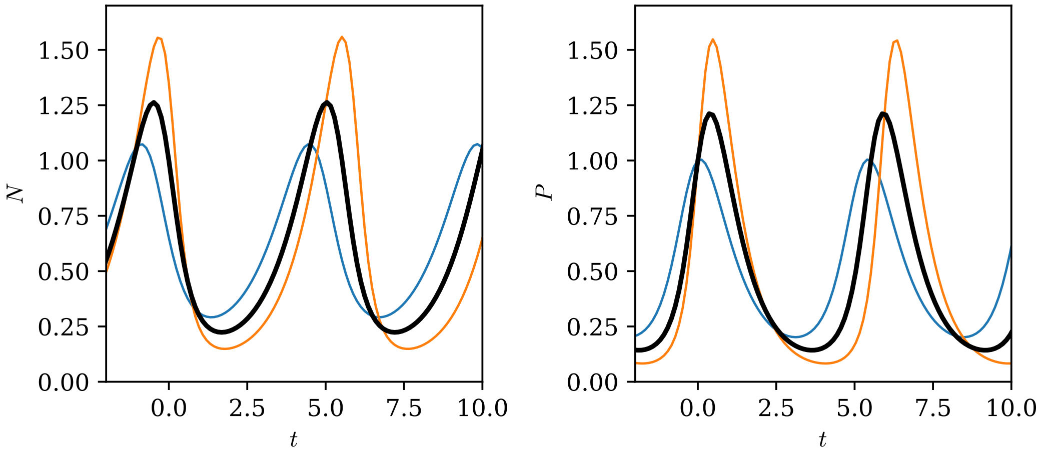

Figure 1.5: Example solutions curves of the Lotka–Volterra predator–prey model with varying initial values for N.

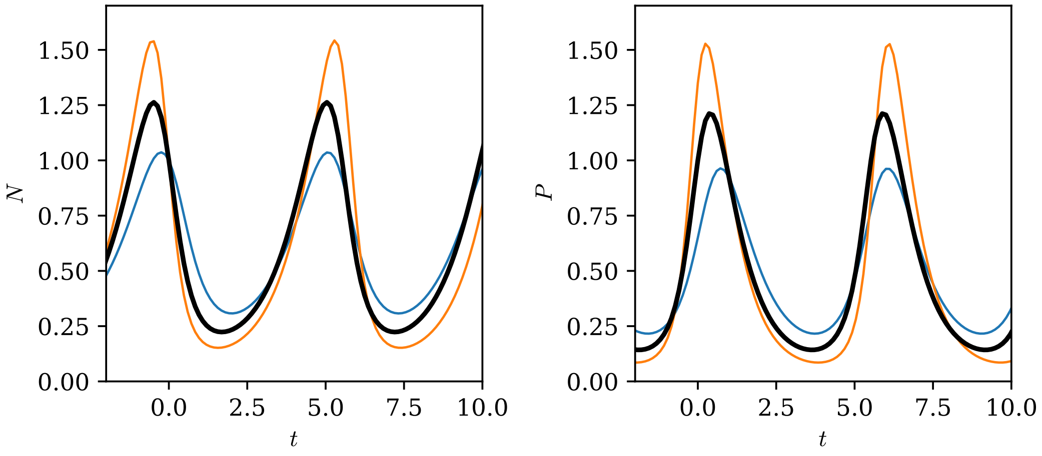

Figure 1.6: Example solutions curves of the Lotka–Volterra predator–prey model with varying initial values for P.

to lactose in *Escherichia coli* with a delay differential equation. Since this thesis only covers ODE:s, the slightly simplified ODE model used in [27] will instead be analyzed, which is modeled by

$$\frac{dM}{dt} = \alpha_M \frac{1 + K_1 A^n}{K + K_1 A^n} + \Gamma_0 - \gamma_M M \tag{1.18a}$$

$$\frac{dB}{dt} = \alpha_B M - \gamma_B B \tag{1.18b}$$

$$\frac{dL}{dt} = \alpha_L P \frac{L_e}{K_{L_e} + L_e} - \beta_{L_1} P \frac{L}{K_{L_1} + L} - \beta_{L_2} B \frac{L}{K_{L_2} + L} - \gamma_L L \tag{1.18c}$$

$$\frac{dA}{dt} = \alpha_A B \frac{L}{K_L + L} - \beta_A B \frac{A}{K_A + A} - \gamma_A A \tag{1.18d}$$

$$\frac{dP}{dt} = \alpha_P M - \gamma_P P, \tag{1.18e}$$

where M is mRNA production, B is the concentration of β-galactosidase, A is the concentration of allolactose, L is the concentration of intracellular lactose and P the concentration of permease.

Chapter 2

The mathematical theory of symmetries

In this chapter, the mathematical theory used in the thesis will be presented. The theory mostly concerns symmetry groups in the setting of ordinary differential equations (ODE:s), and systems thereof. To aid readers new to this subject and with varying familiarity with related mathematical subjects, the theory is presented in a straight forward fashion, avoiding unnecessary generalizations and proofs of most results. The mathematical theory and notation used in this and subsequent chapters is based on the works of three authors. For readers wishing to explore the subject further, the sources are presented here in short.

The first source [28] by Hydon, serves as a great introductory text on the subject of symmetry methods. For readers unfamiliar with the fields of differential geometry and Lie algebras wishing to use methods similar to the ones in this thesis, the book can be helpful for getting off the ground. This is mainly due to fact that theory is only introduced on a need to know basis throughout the book, and as such readers seeking the mathematical rigor lacking in this text will not find it there.

The second sources [29, 30] by Olver, on the other hand treats the subject stringently and serves as good reference points for readers wishing to understand the theory in more depth. While [29] focuses more on the specific application to differential equations, [30] puts more focus on the geometric concepts involved.

The third source [31] by Ovsiannikov, deals with group classification, a slightly more advanced subject on which the technique developed in chapter 4 is based. Roughly, group classification is about finding which specializations of a differential equation with some arbitrary function in its formulation share symmetries. Due to its earlier publication date, the book treats some subjects in a less modern way than the works by Hydon and Olver, and is therefore not recommended for readers unfamiliar with the concerned theory.

The notation in this thesis will be based on the notation in [28], employing partial notational concepts from [30] and [31] when further clarity is desired.

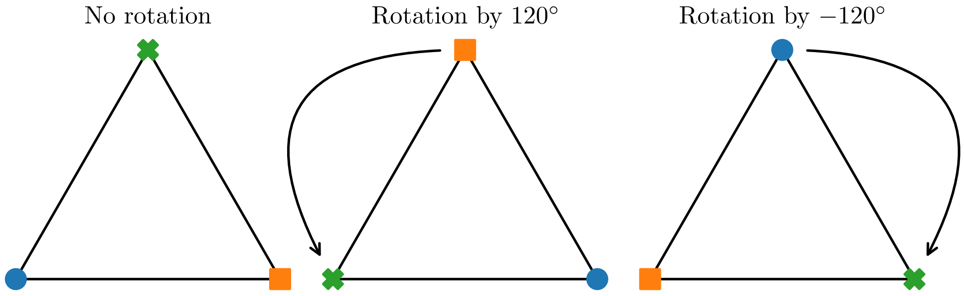

Figure 2.1: Rotational symmetries of an equilateral triangle.

2.1 Point symmetries

In mathematics, a symmetry is a transformation that preserves some structure. The word symmetry is used since the mathematical concept of symmetry encompasses what is meant by symmetry in everyday speech. A symmetric face is a face such that when mirrored it looks the same. Here, mirroring is the transformation and "looking the same" is the structure. In mathematics, however, the structure must be well defined, or in more common language, must be a statement that has a clear distinction between being true or false. The transformation can also be chosen more freely, beyond the transformations usually implied when talking about symmetries in everyday speech.

The most common example of a mathematical symmetry is rotating and flipping a triangle. The structure of the triangle can be stated as the location of all the vertices and the length of the edges between specific vertices. Rotating an equilateral triangle 120 or 240 degrees around its center, as seen in fig. 2.1, will change the location of each individual vertex, but the positions of the set of all vertices will remain the same. Since the edges are unchanged relative to the points, these rotations constitute a symmetry of the triangle. It is worth noting that the rotational transformations map points from the 2-dimensional plane to the two dimensional plane or, stated in mathematical terms, the rotations are mappings $\Gamma : \mathbb{R}^2 \to \mathbb{R}^2$.

In the methods used in this thesis, transformations similar to such a Γ are considered, but the structure of a triangle is instead replaced with the structure of a differential equation. Initially, assume the differential equation is an ODE of the first order and can thus be written on the form

$$\frac{dy}{dx} = \omega(x, y). \tag{2.1}$$

The structure of a first order ODE is thus defined by the function ω. ω is hence related to an infinite set of solutions $u(x)$ that all fulfill the ODE (2.1). Geometrically, a solution (or any scalar function of x for that matter) can be thought of as a set γ_u of points in the xy-plane, which constitutes a curve, for which $y = u(x)$ holds for all x. Not every curve in the xy-plane corresponds to a function however. A curve corresponds to a function if and only if it is transverse to the y-axis, that is: the tangent of the curve never points in only the y-direction. Additionally for a given ODE, every point in the xy-plane belongs to exactly one such curve γ_u: the curve of the solution that runs through that point.

A symmetry of a first order ODE (2.1) is a transformation that preserves the solution curves. This means that if two points (x_1, y_1) and (x_2, y_2) belong to the same solution curve γ, the transformed points $\Gamma(x_1, y_1)$ and $\Gamma(x_2, y_2)$ must belong to the same solution curve, denoted by $\Gamma\gamma$, for the transformation Γ to be a symmetry. This property can be defined as:

Definition 2.1 (Point symmetry)**.** A transformation

$$\Gamma : (x, y) \mapsto (\hat{x}(x, y), \hat{y}(x, y))$$

is a point symmetry of the ODE (2.1) if

$$\frac{dy}{dx} = \omega(x, y) \implies \frac{d\hat{y}}{d\hat{x}} = \omega(\hat{x}, \hat{y}).$$

The "point" in the term "point symmetry" refers to the fact that the transformation Γ only acts on the points belonging to the solution curves and nothing else. This must not always be the case when generalizing the theory, but those generalizations will not be touched upon in this thesis.

2.1.1 Jet spaces

The observant reader might have already noted that there is some need for clarification of definition 2.1. While the transformation Γ treats y as a point in $\mathbb{R}$, the ODE (2.1) treats y as a differentiable function of x, or in other words an element $y(x)$ of the set of once continuously differentiable functions $\mathcal{C}^1(\mathbb{R})$. In many contexts this abuse of notation could be accepted without further remarks, but when using symmetry methods the subtlety of this operation is key to the calculations performed. To avoid confusion while introducing the subject in this subsection, the point representation will be denoted by y while the function representation will be denoted by $f(x)$.

The xy-plane previously mentioned can be seen as consisting of two components: the space of independent variables $B \simeq \mathbb{R}$, also known as the base space, and the space of dependent variables $F \simeq \mathbb{R}$, also known as the fiber.[1] The plane then is the product space $E = B \times F \simeq \mathbb{R}^2$. It is in this plane E, commonly called the total space, that the curves γ live. To be able to formulate first order differential statements, the space $F_1 \simeq \mathbb{R}$ is used. The elements of F_1 will be denoted y' or $y^{(1)}$, implying that the elements correspond to the first derivative $f'(x)$ of the function $f(x)$. It is however important to note that F_1 is no more the space of derivative functions $f'(x)$ than F is the space of once continuously differentiable functions $f(x)$; the implied relation between the two is merely aesthetic so far. Together with the fiber F, F_1 forms the prolonged fiber

---

[1] The symbol $\simeq$ is used here to mean that the space must only be similar to the real numbers. This means that, for example, only the positive real numbers could be used as the space B.

$\underset{1}{F} = F \times F_1$. The prolonged fiber $\underset{1}{F}$ can be combined with the base space B to create $J_1 = J_1E = E \times F_1 = B \times \underset{1}{F} \simeq \mathbb{R}^3$, the first order jet space of E.

All differentiable functions $f : B \to F$ have a unique equivalent function $\underset{1}{f} : B \to \underset{1}{F}$ called the first prolongation of $f(x)$, defined as

$$\underset{1}{f}(x) = \left(f(x), \frac{df}{dx}(x)\right).$$

In extension to this concept, a smooth transverse curve $\gamma \subset E$ has a prolongation which is a curve $\underset{1}{\gamma} \subset J_1$ defined by

$$\underset{1}{\gamma} = \left\{ \left(x, \underset{1}{f}(x)\right) : \quad x \in B \right\},$$

where f is the function corresponding to the curve γ.

Using these tools, the ODE (2.1) can be reformulated using jet spaces. The purpose of the ODE is to define some set of solutions, and as such the reformulation should define that same set of solutions. Using jet-notation, the problem can be formulated as finding curves $\underset{1}{\gamma}$ in J_1 satisfying

$$\Delta(\underset{1}{z}) := y' - \omega(x, y) = 0, \tag{2.2}$$

as well as the condition that the curve is a prolongation of some curve γ corresponding to a continuously differentiable function. The curves γ will then correspond to the solutions $u(x)$ of the ODE (2.1). This can be seen in fig. 2.2, where the prolongations of the solution curves lies on the jet-surface defined by eq. (2.2).

While only first order ODE:s are studied in this thesis, some basic knowledge of symmetry methods for higher order ODE:s is required to be able to understand how the process of finding symmetries differ between first and higher order ODE:s. An ODE of degree k can be written on the form

$$\frac{d^k y}{dx^k} = \omega\left(x, y, \frac{dy}{dx}, \dots, \frac{d^{k-1}y}{dx^{k-1}}\right),$$

while higher order jet spaces $J_k = J_kE$ take the form

$$J_k = B \times F \times F_1 \times \cdots \times F_k$$

with elements

$$\underset{k}{z} = \left(x, y, y', \dots, y^{(k)}\right).$$

An ODE of degree k can thus be formulated as finding curves in J_k that satisfy

$$\Delta(\underset{k}{z}) = y^{(k)} - \omega(x, y, y', \dots, y^{(k-1)}) = 0$$

as well as the condition that the curves should be k:th order prolongations

$$\underset{k}{\gamma_u} = \left\{ \underset{k}{z} = \left(x^*, y, y', \dots, y^{(k)}\right) : \quad y^{(l)} = \frac{d^l u}{dx^l}(x^*), \quad x^* \in B, \quad l = 0, \dots, k \right\}$$

of curves γ corresponding to functions $u(x) \in \mathcal{C}^k(B)$. Here $y^{(0)} = y$ and $\frac{d^0 u}{dx^0} = u(x)$.

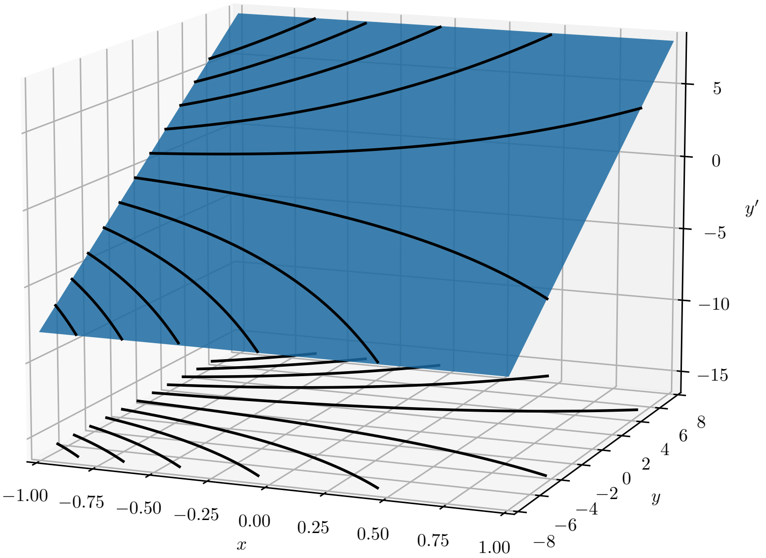

Figure 2.2: The surface $y' = y$, and solution curves to the corresponding differential equation both prolonged to the jet space and projected on the x-y-plane.

2.1.2 The total derivative

Since the jet space J_k treats the variables y, y', …, $y^{(k)}$ as independent coordinates, differentiation in x, denoted as ∂_x, will not affect those terms. While this is the desired behavior of a jet space, there is also a need to be able to mirror the behavior of differentiation of the functions $y(x)$, $y'(x)$, …, $y^{(k)}(x)$ in x. Thus a differential operator

$$D_x = \partial_x + y' \cdot \partial_y + y'' \cdot \partial_{y'} + \cdots + y^{(k+1)} \cdot \partial_{y^{(k)}}$$

on J_k is introduced, called the total derivative. D_x will act on expressions in J_k in the same way that $\frac{d}{dx}$ would act on corresponding expressions consisting of x, $y(x)$ and derivatives of $y(x)$ in x.

A change of variables

$$\begin{aligned}\hat{x} &= \hat{x}(x, y(x))\\ \hat{y} &= \hat{y}(x, y(x)) = \hat{y}(\hat{x})\end{aligned}$$

in the function space can be represented in the jet space using the total derivative. Due to the chain rule,

$$\frac{d\hat{y}}{d\hat{x}} = \frac{\frac{\partial \hat{y}}{\partial x} + \frac{\partial \hat{y}}{\partial y}\frac{dy}{dx}}{\frac{\partial \hat{x}}{\partial x} + \frac{\partial \hat{x}}{\partial y}\frac{dy}{dx}}$$

in the function space. In order to keep the correspondence between the function view and the jet view, viewing the change of variables as a transformation

$$\Gamma : (x, y) \mapsto (\hat{x}(x, y), \hat{y}(x, y)),$$

the first prolongation of that transformation defined by

$$\underset{1}{\Gamma} : (x, y, y') \mapsto \left(\hat{x}(x, y), \hat{y}(x, y), \frac{D_x\,\hat{y}(x, y)}{D_x\,\hat{x}(x, y)}\right)$$

will retain the correspondence to the ODE in the changed variables.

Using the prolongation of the transformation, definition 2.1 of a first order symmetry for the ODE (2.1) can be restated in the first order jet space J_1 for the corresponding eq. (2.2).

Lemma 2.1.1. *A diffeomorphic transformation* $\Gamma : (x, y) \mapsto (\hat{x}(x, y), \hat{y}(x, y))$ *is a point symmetry of the ODE (2.1) if and only if*

$$\frac{\partial_x \hat{y} + \omega(x, y)\partial_y \hat{y}}{\partial_x \hat{x} + \omega(x, y)\partial_y \hat{x}} = \omega(\hat{x}, \hat{y}) \tag{2.3}$$

holds.

Given a transformation Γ, it is therefore easy to check whether it is a point symmetry of the ODE (2.1). The reverse process (finding point symmetries of the ODE (2.1)) is on the other hand not easy, as eq. (2.3) will in all but the most trivial cases result in a non-linear PDE with two unknown functions. However, by restricting attention to a specific type of point symmetries, these conditions can be simplified.

2.2 Lie point symmetries

A common restriction when studying symmetries is to limit the scope of sought symmetries to Lie groups of symmetries. A Lie group is a mathematical group[2], where the members of the group can be parametrized by one or several continuous parameters. A Lie group of transformations on E is thus a group with composition as the operator, where the transformations are parametrized by one or several continuous parameters. If the transformations can be indexed by a single real parameter $\epsilon \in \mathbb{R}$, the Lie group is said to be a one-parameter (real) Lie group of transformations. The transformations in such a Lie group can be parametrized as

$$\Gamma_\epsilon : (x, y) \mapsto (\hat{x}_\epsilon(x, y), \hat{y}_\epsilon(x, y)),$$

where both $\hat{x}_\epsilon(x, y)$ and $\hat{y}_\epsilon(x, y)$ are smooth (and therefore differentiable) in ϵ when fixing x and y. Additionally, the transformation parametrized by $\epsilon = 0$ will be the identity transformation $\Gamma_0 : (x, y) \mapsto (x, y)$.

If all transformations in such a group are symmetries of a differential equation, the group is said to be a Lie point symmetry of the differential equation. The following is a simple example of a one parameter Lie point symmetry.

---

[2] For readers unfamiliar with abstract algebra: a group is a set (collection of elements), together with some operation that is associative. A group must also have an identity element, and all elements must have an inverse. An example of a group is the set of real numbers $\mathbb{R}$, together with the operation + (it is associative since $(a + b) + c = a + (b + c)$). The identity element is then 0, and all elements have inverses (the inverse of a is $-a$).

Example 2.2.1. The ODE

$$\frac{dy}{dx} = y = \omega(x,y) \tag{2.4}$$

has several symmetries. One group of symmetries is

$$\Gamma_\epsilon(x,y) = (\hat{x}_\epsilon(x,y), \hat{y}_\epsilon(x,y)) = (x+\epsilon, y), \quad \forall \epsilon \in \mathbb{R} \tag{2.5}$$

This can be shown by considering eq. (2.4) in the jet space J_1, resulting in

$$\frac{\partial_x \hat{y}_\epsilon + \omega(x,y)\partial_y \hat{y}_\epsilon}{\partial_x \hat{x}_\epsilon + \omega(x,y)\partial_y \hat{x}_\epsilon} = \frac{y}{1} = \hat{y}_\epsilon = \omega(\hat{x}_\epsilon, \hat{y}_\epsilon), \quad \forall \epsilon \in \mathbb{R}.$$

So by lemma 2.1.1 the transformations are point symmetries. By fixing $(x,y) = (x^*, y^*)$,

$$\frac{d}{d\epsilon}\hat{x}_\epsilon(x^*,y^*), \hat{y}_\epsilon(x^*,y^*) = \left(\frac{d\hat{x}^*}{d\epsilon}, \frac{d\hat{y}^*}{d\epsilon}\right) = (1,0)$$

for any (x^*, y^*). This shows that the transformations are smooth in ϵ, and thus constitute a one parameter Lie point symmetry.

While the Lie groups of point symmetries can be parametrized explicitly such as in eq. (2.5), it is more useful to characterize the Lie group by its associated vector field

$$(\xi(x,y), \eta(x,y)),$$

also known as the tangent field of the transformation group. The tangent field can be calculated pointwise by

$$\frac{d}{d\epsilon}\hat{x}_\epsilon(x^*,y^*), \hat{y}_\epsilon(x^*,y^*)\Big|_{\epsilon=0} = (\xi(x^*,y^*), \eta(x^*,y^*))$$

for every fixed point $(x^*, y^*) \in E$. The tangent field can be thought of as the vector field that points in E flow along when the parameter ϵ of transformation Γ_ϵ is increased.

2.2.1 The linearized symmetry condition

Using the tangent field of a one-parameter Lie symmetry group, the symmetry condition as formulated in lemma 2.1.1 can be further simplified.

Lemma 2.2.1. *A one-parameter Lie group of point transformations constitute a Lie point symmetry of the ODE (2.1) if and only if*

$$\partial_x \eta + (\partial_y \eta - \partial_x \xi)\omega - \partial_y(\xi)\omega^2 - \xi \partial_x \omega - \eta \partial_y \omega = 0,$$

where $(\xi(x,y), \eta(x,y))$ *is the tangent field of the Lie group.*

Proof. By lemma 2.1.1, the transformations Γ_ϵ are point symmetries of the ODE (2.1) if and only if

$$\frac{\partial_x \hat{y}(x,y;\epsilon) + \omega(x,y)\partial_y \hat{y}(x,y;\epsilon)}{\partial_x \hat{x}(x,y;\epsilon) + \omega(x,y)\partial_y \hat{x}(x,y;\epsilon)} = \omega(\hat{x}(x,y;\epsilon), \hat{y}(x,y;\epsilon)).$$

Differentiating with respect to ϵ,

$$\frac{\partial_x \frac{d\hat{y}}{d\epsilon} + \omega \partial_y \frac{d\hat{y}}{d\epsilon}}{\partial_x \hat{x} + \omega(x,y)\partial_y \hat{x}} - \frac{\left(\partial_x \frac{d\hat{x}}{d\epsilon} + \omega \partial_y \frac{d\hat{x}}{d\epsilon}\right)(\partial_x \hat{y} + \omega(x,y)\partial_y \hat{y})}{(\partial_x \hat{x} + \omega(x,y)\partial_y \hat{x})^2} - \frac{d\hat{x}}{d\epsilon}\partial_x \omega - \frac{d\hat{y}}{d\epsilon}\partial_y \omega = 0. \quad (2.6)$$

It is sufficient to show that this expression holds at $\epsilon = 0$ for all x and y, since evaluation in any $\tilde{\epsilon} \neq 0$ will be equivalent to the expression for $\epsilon = 0$ in the point $\Gamma_{\tilde{\epsilon}}(x,y)$. Evaluation at $\epsilon = 0$ yields $d\hat{x}/d\epsilon = \xi$ and $d\hat{y}/d\epsilon = \eta$. Additionally, $\hat{x}(x,y;\epsilon)|_{\epsilon=0} = x$ and $\hat{y}(x,y;\epsilon)|_{\epsilon=0} = y$ since the transformation parametrized by $\epsilon = 0$ is always the identity transformation in a one-parameter Lie groups of transformations. Equation (2.6) evaluates to

$$\partial_x \eta + (\partial_y \eta - \partial_x \xi)\omega - \partial_y(\xi)\omega^2 - \xi \partial_x \omega - \eta \partial_y \omega = 0,$$

and hence the proof is complete. □

2.2.2 Invariant solutions and trivial symmetries

An important property of a Lie group of symmetries is which, if any, solution curves γ_u are invariant under all transformations Γ_ϵ. A solution curve being invariant means that the transformed solution curve

$$\Gamma_\epsilon \gamma_u = \{\Gamma_\epsilon z : \quad z \in \gamma_u\}$$

is equal to the solution curve γ_u. It should be noted that this does not mean that every point in γ_u need be transformed to itself; the equivalency must merely hold for the entire set γ_u.

The invariance of a solution can be studied using the characteristic

$$Q(x,y,y') = \eta(x,y) - y'\xi(x,y)$$

of a Lie group of symmetries with tangent field $(\xi(x,y), \eta(x,y))$. The characteristic can be seen as the magnitude of the cross product between the direction of solution curves

$$D_x\,(x,y) = (1, y')$$

and the tangent field. As is known from linear algebra, the cross product of two vectors in three dimensions has magnitude 0 if and only if they are parallel. So if the characteristic is equal to zero in a point x^*, y^*, y'^*, the tangent field is parallel with the tangent of the solution curve in that point. If this hold for all points $(x,y,y') \in \gamma_u$[1], the points of the solution curve γ_u will thus always be transformed to other points of the same solution curve. For a solution γ_u to eq. (2.2)

$$\underset{1}{\gamma_u} = (x, y, \omega(x, y)),$$

and hence the reduced characteristic

$$\bar{Q}(x, y) = \eta(x, y) - \omega(x, y)\xi(x, y)$$

must be equal to 0 for all $(x, y) \in \gamma_u$ for the solution curve γ_u to be invariant under the Lie point symmetry with tangent field $(\xi(x, y), \eta(x, y))$.

A Lie group of symmetries for which all solution curves γ_u of eq. (2.2) are invariant is called a trivial symmetry group. For such a symmetry group, the reduced characteristic will be zero everywhere, or in other words

$$\bar{Q}(x, y) \equiv 0. \tag{2.7}$$

Trivial symmetries are called trivial, since finding one is easy. Simply, let the tangent field $(\xi(x, y), \eta(x, y)) = (1, \omega(x, y))$. The Lie transformation group is a point symmetry group, since lemma 2.2.1 is fulfilled. Furthermore, it is a trivial symmetry group since eq. (2.7) is always fulfilled. Intuitively, a trivial symmetry can be understood as a group of transformations that transforms points along the solution curves of the ODE.

2.3 Generalization to higher orders and systems

The theory so far discussed has dealt with single ODE:s of the first order. Most systems of interest are however not modeled in this way. As mentioned earlier, the theory can be extended to deal with higher order ODE:s. Additionally, many other types of differential equations can be treated with further generalizations, among them systems of ODE:s. In this section the previously stated theory will be generalized to include both higher order ODE:s and systems of first order ODE:s. The motivation for these generalizations are quite different.

The generalization to higher order ODE:s will as previously mentioned be used as a foil for the theory used in this thesis. As it turns out, first order ODE:s are quite unique in that there is no clear process to find all the symmetries of the ODE:s. Since the theory of symmetries of differential equations in applications has mostly developed around physics, a subject where higher order differential equations are the norm, the theoretical methods for finding symmetries of first order differential equations are not as mature in the literature as compared to those for higher order equations. In this thesis the limitations of techniques for first order ODE:s play a large role, and it is therefore important for the reader to understand the context in which this discussion occurs.

On the other hand, the generalization to systems of ODE:s is purely practically motivated, as most biological systems are modeled with several interacting states. Throughout this subsection both generalizations will be presented simultaneously, as the required notation for the respective generalizations are more intuitive in tandem. In this section, fewer intuitive explanations for the calculations are used, as the higher dimensional geometry make such explanations harder to grasp. It will therefore be useful for the reader to have the first order equivalents of the theory in mind to enhance intuition.

2.3.1 The infinitesimal generator and prolongations

To simplify the notation a differential operator

$$X = \xi(x, y)\partial_x + \eta(x, y)\partial_y$$

called an infinitesimal generator of the symmetry group with tangent field (ξ, η), can be introduced. The infinitesimal generator acts on functions $\phi : E \to S$ where S is a vector space, and returns the action of the tangent field (ξ, η) of a Lie point symmetry with elements Γ_ϵ on the function. The action gives a measure of the change in ϕ when continuously transforming the plane which it acts on, since

$$\frac{d}{d\epsilon}\phi \circ \Gamma_\epsilon \bigg|_{\epsilon=0} = X\phi.$$

Just as the tangent field characterizes the Lie point symmetry, so does the infinitesimal generator, as it depends uniquely on the tangent field.

The infinitesimal generator can be prolonged, still entirely defined by ξ and η, to act on functions in any given jet space J_k. Here the requirement of the prolongation $\underset{k}{X}$ is that it should be the infinitesimal generator of the prolonged Lie point transformations $\underset{k}{\Gamma_\epsilon}$. Or in other words, for any function $\psi : J_k \to S$,

$$\frac{d}{d\epsilon}\psi \circ \underset{k}{\Gamma_\epsilon} \bigg|_{\epsilon=0} = \underset{k}{X}\psi.$$

For first order ODE:s the jet space is J_1, and thus the first prolongation is needed, which takes the form

$$\underset{1}{X} = \xi(x, y)\partial_x + \eta(x, y)\partial_y + \eta_{(1)}(x, y)\partial_{y'},$$

where

$$\eta_{(1)}(x, y) = \eta_x(x, y) + (\eta_y(x, y) - \xi_x(x, y))y' - \xi_y(x, y)(y')^2,$$

where the subscripts of x and y denote the partial derivatives ∂_x and ∂_y. The linearized symmetry condition in lemma 2.2.1 can hence be rewritten using the infinitesimal operator.

Lemma 2.3.1. *A Lie group of point transformations is a symmetry of the ODE (2.1) if and only if*

$$\underset{1}{X}(y' - \omega(x, y))\bigg|_{y'=\omega(x,y)} = 0, \tag{2.8}$$

where $\underset{1}{X}$ *is the first prolongation of the infinitesimal generator of the Lie group of point transformations.*

On this form, the linearized symmetry condition is easier to interpret: Since the transformations of solution curves must be solution curves in order for the transformations to be a symmetry group, the value of $\Delta(\underset{1}{z}) = y' - \omega(x, y) = 0$ must not change. By evaluating the expression at $y' = \omega(x, y)$, it is ensured that this holds for any solution to the ODE (2.1).

By finding further prolongations of X, the linearized symmetry condition can be extended to ODE:s of higher degrees. The k:th order prolongation of the infinitesimal generator is

$$\underset{k}{X} = \xi(x, y)\partial_x + \eta(x, y)\partial_y + \eta_{(1)}(x, y)\partial_{y'} + \cdots + \eta_{(k)}(x, y)\partial_{y^{(k)}}$$

where $\eta_{(k)}$ is defined recursively by

$$\begin{aligned} \eta_{(0)} &= \eta \\ \eta_{(k)}(x, y) &= D_x\left(\eta_{(k-1)}\right) - y^{(k)} D_x\, \xi. \end{aligned}$$

Lemma 2.3.1 will hold for higher order ODE:s, given that y' is replaced by $y^{(k)}$ and $\omega(x, y)$ with $\omega(\underset{k-1}{z})$, and that the infinitesimal generator is prolonged to the k:th degree.

The infinitesimal generator also holds as a valid construction for systems of ODE:s. A system of s first order ODE:s has the form

$$\begin{aligned} y^1_x &= \omega^1(x, y^1, \ldots, y^s) \\ &\vdots \\ y^s_x &= \omega^s(x, y^1, \ldots, y^s), \end{aligned} \tag{2.9}$$

which can be seen as existing in the jet space $J_1 = J_1 E = B \times F \times F_1$ with coordinates

$$\begin{aligned} x &\in B \simeq \mathbb{R} \\ \left(y^1, \ldots, y^s\right) &\in F \simeq \mathbb{R}^s \\ \left(y^1_x, \ldots, y^s_x\right) &\in F_1 \simeq \mathbb{R}^s. \end{aligned}$$

Elements in the total space $E = B \times F$ can similarly to before be denoted $z = (x, \boldsymbol{y})$, where the vector notation $\boldsymbol{y} = \left(y^1, \ldots, y^s\right)$ is used. Equation (2.9) can be written more succinctly as

$$\boldsymbol{y}_x = \boldsymbol{\omega}(z), \tag{2.10}$$

where

$$\begin{aligned} \boldsymbol{y}_x &= \left(y^1_x, \ldots, y^s_x\right) \\ \boldsymbol{\omega}(z) &= \left(\omega^1(z), \ldots, \omega^s(z)\right). \end{aligned}$$

The tangent fields of transformations on E take the form

$$\left(\xi(z), \eta^1(z), \ldots, \eta^s(z)\right)$$

and the infinitesimal generator thus has the form

$$X = \xi(z)\partial_x + \eta^1(z)\partial_{y^1} + \cdots + \eta^s(z)\partial_{y^s} = \xi(z)\partial_x + \boldsymbol{\eta}(z)\cdot\partial_{\boldsymbol{y}},$$

once again employing the vector notation

$$\begin{aligned}\boldsymbol{\eta}(z) &= \Big(\eta^1(z), \dots, \eta^s(z)\Big)\\ \partial_{\boldsymbol{y}} &= \Big(\partial_{y^1}, \dots, \partial_{y^s}\Big)\end{aligned}$$

to shorten the expression. The infinitesimal generator can be prolonged by defining

$$\eta^k_{(1)}(x,y) = D_x\,\eta^k - y' D_x\,\xi,$$

where the total derivative is defined as

$$D_x \; = \partial_x + y^1_x \cdot \partial_{y^1} + \cdots + y^s_x \cdot \partial_{y^s} + \dots$$

(the second dots are due to the fact that the total derivative technically acts on the derivatives of the y^k:s, which does not concern us).

Using these tools, the earlier results for scalar ODE:s are easy to reformulate for first order systems of ODE:s, and whose generalization to higher order (systems of) ODE:s should be clear.

Definition 2.2 (Point symmetry)**.** A transformation

$$\Gamma : z \mapsto \hat{z}(z)$$

is a point symmetry of a system of first order ODE:s (2.10) if

$$\frac{d\boldsymbol{y}}{dx} = \boldsymbol{\omega}(z) \implies \frac{d\hat{\boldsymbol{y}}}{d\hat{x}} = \boldsymbol{\omega}(\hat{z}).$$

Theorem 2.3.2. *A one-parameter Lie group of point transformations constitute a Lie point symmetry of eq.* (2.10) *if and only if*

$$\underset{1}{X}(\boldsymbol{y}_x - \boldsymbol{\omega}(z))\bigg|_{\boldsymbol{y}_x = \boldsymbol{\omega}(z)} = 0,$$

where X is the infinitesimal generator of the Lie group.

2.3.2 Trivial symmetries of first order systems

The concept of trivial symmetries can also be generalized, but only for systems of first order ODE:s. The reason for this is quite simple: if a higher order ODE had a symmetry which was trivial, all solutions of the ODE would flow along the tangent field of the symmetry. But since the tangent field of a Lie point symmetry only depends on the total space, that would mean that there was an expression for the first derivative of all solution curves of the ODE only dependent on the total space. Thus the ODE would not truly be of higher order, as it could be rewritten as a first order ODE. This fact is not of great concern here, as this thesis only deals with first order systems.

For a system of ODE:s, the characteristic becomes a function

$$\boldsymbol{Q}(\underset{1}{z}) = \left(Q^1(\underset{1}{z}), \ldots, Q^s(\underset{1}{z})\right)$$

with components defined by

$$Q^k(\underset{1}{z}) = \eta^k(z) - y_x^k \xi(z), \quad k = 1, \ldots, s.$$

A solution curve γ_u of a system of ODE:s is an invariant of a symmetry with characteristic $\boldsymbol{Q}$ if

$$Q^k(\underset{1}{z}) = 0, \quad \forall z \in \gamma_u.$$

For a system of first order ODE:s (2.10) the condition can be simplified, using the reduced characteristic $\bar{\boldsymbol{Q}}(z) = \boldsymbol{Q}(z, \boldsymbol{\omega}(z))$, to

$$\bar{Q}^k(z) = \eta^k(z) - \omega^k(z)\xi(z) = 0, \quad \forall z \in \gamma_u.$$

The concept of a trivial symmetry can thus be generalized to first order systems.

Definition 2.3 (Trivial symmetry)**.** A Lie point symmetry with tangent field $(\xi, \boldsymbol{\eta})$ is a trivial symmetry of a system of first order ODE:s (2.10) if

$$\bar{\boldsymbol{Q}}(z) \equiv 0.$$

2.4 Properties of Lie point symmetries

Before moving on to the process of finding symmetries, some further results are of interest in order to better understand and interpret the symmetries found. Up until this point, the definition of a Lie group has been consciously avoided. This is mainly due to the fact that the specifics are quite involved, and do not play a large role in finding symmetries of the type found in this thesis. To evaluate the results of such calculations, however, some of this theory must be explained. Since a complete understanding of the theory is neither necessary nor viable in this thesis, only the aspects relevant to calculations will be explained. Readers wishing to understand the theory itself are once again recommended [29, 30] as discussed in the beginning of this chapter.

2.4.1 Lie groups and Lie algebras

So far, only one-parameter Lie groups of transformations have been considered. In practice, the collection of all symmetry transformations of a differential equation will almost always include a multiparameter Lie group of transformations. An n-parameter Lie group is a group that also has the structure of an n-dimensional smooth manifold.

The Lie group being a group means that it has elements, and those elements can be multiplied together in some manner. When the group G has transformations $\Gamma : E \to E$ as elements, the multiplication is defined as the composition $\circ$ of elements, defined by

$$\Gamma \circ \tilde{\Gamma} : z \mapsto \Gamma\Big(\tilde{\Gamma}(z)\Big), \tag{2.11}$$

where $\Gamma, \tilde{\Gamma} \in G$. The Lie group having the structure of an n-dimensional smooth manifold means that operations such as differentiation of the elements are defined. This structure appears earlier in this chapter when differentiation $\frac{d}{d\epsilon}$ in the parameter of the one-parameter Lie group was used.

Just as a one-parameter Lie group of transformations is characterized by an infinitesimal generator, an n-parameter Lie group can be characterized by a basis of n infinitesimal generators. For an n-parameter Lie group of transformations with basis $X_1, \ldots, X_n$, the action at a given point can always be represented as

$$X = c_1 X_1 + \cdots + c_n X_n,$$

where $c_1, \ldots, c_n$ are constants. The basis can be seen as the available directions in which a derivative can be taken, in the same way that a partial derivative in multivariate calculus can be taken in an arbitrary direction given by a vector constructed from a set of base vectors.

It is of interest to be able to determine if a multiparameter Lie group of transformations is a symmetry of a differential equation. Equation (2.10) can as in the scalar case be rewritten as

$$\boldsymbol{\Delta}(\underset{1}{z}) = \boldsymbol{y}_x - \boldsymbol{\omega}(z) = 0 \tag{2.12}$$

for the sake of convenience. Let X_1 and X_2 be the infinitesimal generators of two one-parameter Lie point symmetries of eq. (2.12). A two-parameter Lie group of transformations with the basis X_1, X_2 will also be a Lie point symmetry, since

$$\underset{1}{(c_1 X_1 + c_2 X_2)}(\boldsymbol{\Delta}(\underset{1}{z}))\Big|_{\boldsymbol{\Delta}(\underset{1}{z})=0} = c_1 \underset{1}{X_1}(\boldsymbol{\Delta}(\underset{1}{z}))\Big|_{\boldsymbol{\Delta}(\underset{1}{z})=0} + c_2 \underset{1}{X_2}(\boldsymbol{\Delta}(\underset{1}{z}))\Big|_{\boldsymbol{\Delta}(\underset{1}{z})=0} = 0$$

at any point $z \in E$. This argument extends to any multiparameter Lie group of transformations, as it is only dependent on the fact that the infinitesimal generator is a linear differential operator. Thus an n-parameter Lie group of transformations is a symmetry group if the one-parameter Lie groups corresponding to its bases are symmetries.

However, an n-parameter Lie symmetry can not be constructed from the infinitesimal generators of an arbitrary collection of one-parameter Lie symmetries. The fact that a one-parameter Lie group always can be constructed from an infinitesimal generator is a trivial case of a more general requirement. The correspondence between Lie groups of transformations and infinitesimal generators is a special case of a more general correspondence between Lie groups and Lie algebras. Every Lie algebra is equipped with an operation called the Lie bracket, which for the infinitesimal generators is defined as

$$[X_1, X_2] = (X_1(\xi_2) - X_2(\xi_1))\partial_x + (X_1(\boldsymbol{\eta}_2) - X_2(\boldsymbol{\eta}_1)) \cdot \partial_{\boldsymbol{y}},$$

where $X_1 = \xi_1 \partial_x + \boldsymbol{\eta}_1 \cdot \partial_{\boldsymbol{y}}$ and $X_2 = \xi_2 \partial_x + \boldsymbol{\eta}_2 \cdot \partial_{\boldsymbol{y}}$. A Lie algebra is closed under the Lie bracket, which means that

$$[X_1,\, X_2] \in \mathfrak{g}, \quad \forall X_1, X_2 \in \mathfrak{g} \tag{2.13}$$

if $\mathfrak{g}$ is a Lie algebra. The Lie bracket is a bilinear operator, so it is not necessary to check that eq. (2.13) holds for any $X_1, X_2 \in \mathfrak{g}$; rather it is enough to ensure that eq. (2.13) holds for the elements of a basis $X_1, \ldots, X_n$ of $\mathfrak{g}$. If that is the case, any $X_1, X_2 \in \mathfrak{g}$ can be written as linear combinations $X = c_1 X_1 + \cdots + c_n X_n$, and will thus be closed under the Lie bracket.

All Lie algebras have a corresponding Lie group, so in order to generalize the correspondence between Lie groups of transformations and infinitesimal generators the requirement becomes that a Lie algebra $\mathfrak{g}$, with the basis $X_1, \ldots, X_n$, always has a corresponding $n-$-parameter Lie group of transformations. For one-dimensional Lie algebras this correspondence was seen as trivial, since the Lie algebra $\mathfrak{g}$ only has one base generator, and the group must be closed under the Lie bracket since

$$[X,\, X] = 0 \in \mathfrak{g}$$

for any generator X and any group $\mathfrak{g} = \{cX \,:\, c \in \mathbb{R}\}$ generated by X.

2.4.2 The structure of the group of all symmetries of first order ODE:s

Every infinitesimal generator X with corresponding tangent field $(\xi, \boldsymbol{\eta})$ can, given a system of ODE:s (2.12), be written on the form

$$X = \xi \partial_x + \left(\xi \boldsymbol{\omega} + \bar{\boldsymbol{Q}}\right) \cdot \partial_{\boldsymbol{y}},$$

where $\bar{\boldsymbol{Q}}$ is the reduced characteristic. Considering the infinitesimal generators

$$X_{\mathrm{T}} = \partial_x + \boldsymbol{\omega} \cdot \partial_{\boldsymbol{y}} \tag{2.14a}$$

$$X_{\bar{\boldsymbol{Q}}} = \bar{\boldsymbol{Q}} \cdot \partial_{\boldsymbol{y}}, \tag{2.14b}$$

X can thus be decomposed into

$$X = \xi X_{\mathrm{T}} + X_{\bar{\boldsymbol{Q}}} \tag{2.15}$$

The linearized symmetry condition 2.3.2 then simplifies to

$$\bar{Q}^k_x + \boldsymbol{\omega} \cdot \bar{Q}^k_{\boldsymbol{y}} - \bar{\boldsymbol{Q}} \cdot \omega^k_{\boldsymbol{y}} = 0, \quad k = 1, \ldots, s. \tag{2.16}$$

Using the Lie bracket, eq. (2.16) can be further simplified to

$$\left[X_{\mathrm{T}},\, X_{\bar{\boldsymbol{Q}}}\right] = 0. \tag{2.17}$$

This formulation reveals several properties of the space of all Lie point symmetries for first order systems of ODE:s (2.12).

The first result concerns the trivial symmetries of a first order ODE. If X is a trivial symmetry, $X_{\bar{\boldsymbol{Q}}} = 0$ since $\bar{\boldsymbol{Q}} = 0$. Since eq. (2.17) always holds if $X_{\bar{\boldsymbol{Q}}} = 0$, a one-parameter Lie point transformation is a trivial symmetry of eq. (2.12) if and only if

$$X = \xi X_{\mathrm{T}}$$

for any function $\xi : E \to \mathbb{R}$. Given two arbitrary trivial symmetry generators ξX_{T} and $\tilde{\xi} X_{\mathrm{T}}$, the Lie bracket of the two is

$$\Big[\xi X_{\mathrm{T}},\, \tilde{\xi} X_{\mathrm{T}}\Big] = \Big(\xi \tilde{\xi}_x + \xi \boldsymbol{\omega} \cdot \tilde{\xi}_{\boldsymbol{y}} - \tilde{\xi} \xi_x - \tilde{\xi} \boldsymbol{\omega} \cdot \xi_{\boldsymbol{y}}\Big) X_{\mathrm{T}},$$

which in turn is a trivial symmetry generator. Hence, the set of all trivial symmetry generators form an algebra of their own, denoted $\mathfrak{g}^{\infty}$. $\mathfrak{g}^{\infty}$ is a subalgebra of the Lie algebra $\mathfrak{g}$ of all infinitesimal generators corresponding Lie point symmetries of eq. (2.12), since its elements are a subset of all elements in $\mathfrak{g}$, and $\mathfrak{g}^{\infty}$ in itself is an algebra. Similarly, all symmetry generators on the form $\boldsymbol{\eta} \cdot \partial_{\boldsymbol{y}} = \bar{\boldsymbol{Q}} \cdot \partial_{\boldsymbol{y}}$ form a subalgebra $\mathfrak{g}^0$, since

$$[\boldsymbol{\eta} \cdot \partial_{\boldsymbol{y}},\, \tilde{\boldsymbol{\eta}} \cdot \partial_{\boldsymbol{y}}] = \Big(\boldsymbol{\eta} \cdot \tilde{\eta}^1_{\boldsymbol{y}} - \tilde{\boldsymbol{\eta}} \cdot \eta^1_{\boldsymbol{y}}\Big) \partial_{y^1} + \cdots + \Big(\boldsymbol{\eta} \cdot \tilde{\eta}^s_{\boldsymbol{y}} - \tilde{\boldsymbol{\eta}} \cdot \eta^s_{\boldsymbol{y}}\Big) \partial_{y^s}$$

for arbitrary functions $\boldsymbol{\eta}, \tilde{\boldsymbol{\eta}} : E \to \mathbb{R}^s$ The decomposition in eq. (2.15) can thus be rewritten in more algebraic language as the fact that the algebra of all Lie point symmetries $\mathfrak{g}$ can be written as the direct sum

$$\mathfrak{g} = \mathfrak{g}^{\infty} \oplus \mathfrak{g}^0$$

of subalgebras. Additionally, given an arbitrary infinitesimal generator $X = \xi X_{\mathrm{T}} + X_{\bar{\boldsymbol{Q}}} \in \mathfrak{g}$ and an arbitrary trivial Lie point symmetry generator $\tilde{\xi} X_{\mathrm{T}} \in \mathfrak{g}^{\infty}$, the Lie bracket of the two

$$\begin{aligned} \Big[X,\, \tilde{\xi} X_{\mathrm{T}}\Big] &= \Big[\xi X_{\mathrm{T}},\, \tilde{\xi} X_{\mathrm{T}}\Big] + \Big[X_{\bar{\boldsymbol{Q}}},\, \tilde{\xi} X_{\mathrm{T}}\Big] = \\ &= \Big[\xi X_{\mathrm{T}},\, \tilde{\xi} X_{\mathrm{T}}\Big] + \bar{\boldsymbol{Q}} \cdot \tilde{\xi}_{\boldsymbol{y}} X_{\mathrm{T}} + \tilde{\xi} \Big[X_{\bar{\boldsymbol{Q}}},\, X_{\mathrm{T}}\Big] = \Big[\xi X_{\mathrm{T}},\, \tilde{\xi} X_{\mathrm{T}}\Big] + \bar{\boldsymbol{Q}} \cdot \tilde{\xi}_{\boldsymbol{y}} X_{\mathrm{T}} \end{aligned}$$

is a trivial Lie point symmetry generator; in algebraic language $\mathfrak{g}^{\infty}$ is an ideal of $\mathfrak{g}$. Hence, the trivial component of any symmetry can safely be ignored when studying the structure of the Lie algebra $\mathfrak{g}$, corresponding to the Lie group of all Lie point symmetries of eq. (2.12), since the trivial component will only contribute to the trivial (and therefore known) part of the structure.

The second, and far less trivial result from formulation (2.17) of the linearized symmetry condition concerns the structure of the subalgebra $\mathfrak{g}^0$ containing the non-trivial components of all symmetries of eq. (2.12). Finding this structure is analogous to finding all functions $\bar{\boldsymbol{Q}} : E \to \mathbb{R}^s$ solving eq. (2.17), or in other words finding all reduced characteristics corresponding to Lie point symmetries of eq. (2.12). To state this result, two definitions are required.

The first definition relates to a generalization of the concept of invariants.

Definition 2.4 (Invariant function)**.** A function

$$\boldsymbol{I} : E \to \mathbb{R}^n$$

is an invariant of a vector field corresponding to the infinitesimal generator X if and only if

$$X(\boldsymbol{I}) \equiv 0.$$

For a first order ODE, there is an equivalent vector field with corresponding infinitesimal generator X_T as defined in eq. (2.14a). A function $\boldsymbol{I}$ is called an invariant of a first order ODE if it is an invariant of its corresponding vector field.

The second definition relates to how those invariants can be combined.

Definition 2.5 (Functional independence)**.** The functions

$$\boldsymbol{F_i} : E \to \mathbb{R}, \quad i = 1, \dots, n$$

are called functionally dependent if there for each $z_0 \in E$ exists a neighborhood U and a smooth function $h : \mathbb{R}^n \to \mathbb{R}$ that is not identically zero on any subset of $\mathbb{R}^n$, such that

$$h(F_1(z), \dots, F_n(z)) = 0, \quad \forall z \in U.$$

The functions are called functionally independent if they are not functionally dependent when restricted to any open subset of E.

Functional independence thus serves as a generalization of linear independence: if the function h is restricted to being linear, the definition will be equivalent to that of linear independence. It can be proven that given a function $\boldsymbol{J}(x, \boldsymbol{y}) = (J_1(x, \boldsymbol{y}), \dots, J_n(x, \boldsymbol{y}))$ consisting of the functionally independent invariants $J_1, \dots, J_n$ of a vector field on $E \simeq \mathbb{R}^{n+1}$, any invariant $\boldsymbol{I}$ of that same vector field can be written as

$$\boldsymbol{I}(x, \boldsymbol{y}) = h(\boldsymbol{J}(x, \boldsymbol{y})),$$

where h is a smooth function.[3] Such a function $\boldsymbol{J}$ can hence be seen as a “basis” with dimension n for the invariants of a vector field on the $(n+1)$-dimensional space E.[4]

Using these definitions, the following result pertaining to the solutions of eq. (2.17) can be established.

Theorem 2.4.1. *Let* $\boldsymbol{J}(x, \boldsymbol{y}) = (J_1(x, \boldsymbol{y}), \dots, J_s(x, \boldsymbol{y}))$ *consist of the functionally independent invariants* $J_1, \dots, J_s$*. A function* $\bar{\boldsymbol{Q}}$ *is a solution of eq.* (2.17) *if and only if*

$$\partial_{\boldsymbol{y}} \boldsymbol{J} \cdot \bar{\boldsymbol{Q}}$$

is an invariant of the vector field corresponding to the infinitesimal generator X_T*.*

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[3] In [31] such a function J is called a “universal invariant” This term is however also used for the mathematical concept of a u-invariant [32], and will therefore be avoided here.

[4] The invariants will not constitute a basis in the sense of a basis for a function space, but the intuition behind them forming a “basis” will be useful in the scope of this thesis.

Here $\partial_{\boldsymbol{y}} \boldsymbol{J}$ will for all intents and purposes be the Jacobian of J, excluding the derivative in x. It can also be established that $\partial_{\boldsymbol{y}} \boldsymbol{J}$ is invertible, and thus a general form for the functions $\bar{\boldsymbol{Q}}$ that are solutions to eq. (2.17) exists.

Corollary 2.4.2. *A function* $\bar{\boldsymbol{Q}} : E \to \mathbb{R}^s$ *is a solution to eq.* (2.17) *if and only if*

$$\bar{\boldsymbol{Q}} = (\partial_{\boldsymbol{y}} \boldsymbol{J})^{-1} \cdot \boldsymbol{I},$$

where $\boldsymbol{J}(x, \boldsymbol{y}) = (J_1(x, \boldsymbol{y}), \ldots, J_s(x, \boldsymbol{y}))$ *consists of the functionally independent invariants* $J_1, \ldots, J_s$ *and* $\boldsymbol{I} : E \to \mathbb{R}^s$ *is an arbitrary invariant of the vector field corresponding to the infinitesimal generator* X_T.

Chapter 3

Finding symmetries using ansätze

Finding symmetries of first order ODE:s is as previously stated different than finding symmetries of higher order models. For the sake of simplicity, the problem will be shown for scalar explicit ODE:s, or in other words ODE:s on the form

$$y_{(n)} = \omega(\underset{n-1}{z}), \tag{3.1}$$

where $y_{(n)}$ is the n:th derivative in x. Since eq. (3.1) is of degree n, the linearized symmetry condition is

$$\underset{n}{X}(y_{(n)} - \omega(\underset{n-1}{z}))\Big|_{y_{(n)}=\omega(\underset{n-1}{z})} = 0. \tag{3.2}$$

Equation (3.2) is a partial differential equation (PDE) of degree n in the functions $\xi(x, y), \eta(x, y)$. The highest order jet variable $y_{(n)}$ will not be present anywhere in eq. (3.2) as the evaluation on eq. (3.1) removes all such dependence. For an ODE of degree $n > 1$, jet variables $y_{(1)}, \dots, y_{(n-1)}$ will still be present in eq. (3.2), and since neither ξ nor η has any dependence on those variables the equation can be decomposed in those variables. This means that eq. (3.2) will be turned into a system of PDE:s, still of degree n in the functions $\xi(x, y), \eta(x, y)$, called the determining equations of the symmetries. In general, such a system is solvable and thus all symmetries of the systems can be calculated. Much theory in the literature is built around the assumption that the determining equations exist, and that they (at least in theory) can be solved.

For an ODE of degree $n = 1$ such a decomposition is not possible, since no jet variables except for x and y are present in eq. (3.2). Instead, the “determining equations” is the same equation as the linearized symmetry condition. The common solution to this problem is to use an ansatz for the tangent field ξ, η that turns the linearized symmetry condition into a solvable system. Except for some common ansätze like polynomial dependence in one or more variables, coming up with a good ansatz comes down to intuition and luck. In this chapter symmetries of the biological models outlined in chapter 1, all of which are of first order, are found using such ansätze.

3.1 The Hill equation

In this section, Lie point symmetries for the Hill equation will be calculated. Since this work has already been done in [9], this will serve as a reproduction of their results. The calculations are included here as an introduction to the basics of using an ansatz.

3.1.1 A useful infinitesimal generator

The Hill equation

$$y_\tau = -\frac{y^n}{1+y^n} = \omega_n(\tau, y), \quad n > 0. \tag{3.3}$$

clearly has at least the Lie symmetry generator $X = \partial_\tau$. This can be seen by observing that eq. (3.3) has no dependence on τ (since the equation exists in the jet space J_1 where y and y_τ are independent of τ). However, one purpose of finding symmetries of differential equations is to distinguish between models. Since the symmetry $X = \partial_\tau$ holds for all n, it can not be used to compare different degrees of Hill equations. Thus, finding an additional one-parameter Lie symmetry group of the Hill equation is therefore of interest.

The tangent fields of many Lie symmetries of ODE:s are linear in y. The Ansatz

$$(\xi(\tau, y), \eta(\tau, y)) = (A(\tau) + B(\tau)y, C(\tau) + D(\tau)y)$$

is therefore used. Inserting the Ansatz into eq. (2.8), and using the fact that $y' = -y^n/(1+y^n)$, gives that

$$(C' + D'y) + (A' + B'y - D)\frac{y^n}{1+y^n} - B\frac{y^{2n}}{(1+y^n)^2} = -n(C + Dy)\frac{y^{n-1}}{(1+y^n)^2}.$$

Multiplication with $(1+y^n)^2$ in turn gives that

$$(C' + D'y)(1+y^n)^2 + (A' + B'y - D)y^n(1+y^n) - By^{2n} = -n(C+Dy)y^{n-1}. \tag{3.4}$$

The equation can then be separated by powers of y into a system of equations. However, since n is specified to be positive, care must be taken to ensure that the separation holds for all $n > 0$.

Case of $n \neq 1, 2$

When $n > 0$ and $n \neq 1, 2$, all of the possible powers of y will be different. Equation (3.4) can the be separated into the system

$$y^0: \qquad C'(\tau) = 0 \tag{3.5a}$$

$$y^1: \qquad D'(\tau) = 0 \tag{3.5b}$$

$$y^{n-1}: \qquad 0 = -nC(\tau) \tag{3.5c}$$

$$y^n: \qquad 2C'(\tau) + A'(\tau) - D(\tau) = -nD(\tau) \tag{3.5d}$$

$$y^{n+1}: \qquad 2D'(\tau) + B'(\tau) = 0 \tag{3.5e}$$

$$y^{2n}: \qquad C'(\tau)A'(\tau) - D(\tau) - B(\tau) = 0 \tag{3.5f}$$

$$y^{2n+1}: \qquad D'(\tau) + B'(\tau) = 0. \tag{3.5g}$$

From eq. (3.5c)

$$C(\tau) = 0,$$

which renders eq. (3.5a) irrelevant. Equation (3.5b) gives

$$D(\tau) = c_1$$

for a constant c_1 (constants will henceforth be denoted c_i). Equation (3.5d) can be reduced to

$$A'(\tau) = (1 - n)c_1,$$

which means that

$$A(\tau) = c_2 + (1 - n)c_1\tau.$$

Using eq. (3.5e),

$$B(\tau) = c_3,$$

which in turn renders eq. (3.5g) irrelevant. Lastly, eq. (3.5f) can be reduced to

$$(1 - n)c_1 - c_1 - c_3 = 0,$$

which means that

$$c_3 = -nc_1.$$

All tangent fields given the ansatz must therefore be on the form

$$(\xi_n(\tau, y), \eta_n(\tau, y)) = (c_2 + c_1((1 - n)\tau - ny), c_1 y). \tag{3.6}$$

Case of $n = 1$

When $n = 1$ several pairs of powers of y become equal. $y^0 = y^{n-1}$, $y^1 = y^n$ and $y^{n+1} = y^{2n}$. Equation (3.4) is therefore separated into the system

$$y^0: \qquad C'(\tau) = -C(\tau) \tag{3.7a}$$

$$y^1: \qquad D'(\tau) + 2C'(\tau) + A'(\tau) - D(\tau) = -D(\tau) \tag{3.7b}$$

$$y^2: \qquad 2D'(\tau) + B'(\tau) + C'(\tau) + A'(\tau) - D(\tau) - B(\tau) = 0 \tag{3.7c}$$

$$y^3: \qquad D'(\tau) + B'(\tau) = 0. \tag{3.7d}$$

Using eq. (3.7d), the relation

$$D(\tau) = -B(\tau) + c_1 \tag{3.8}$$

can be established. Equation (3.7a) leads to

$$C(\tau) = c_2 e^{-\tau}. \tag{3.9}$$

Subtracting eq. (3.7b) from eq. (3.7c) leads to the equation

$$D'(\tau) + B'(\tau) - C'(\tau) - B(\tau) = D(\tau),$$

which by using eqs. (3.8) and (3.9) can be simplified to

$$c_2 e^{-\tau} = c_1.$$

This only holds if $c_1 = c_2 = 0$ so

$$C(\tau) = 0 \tag{3.10}$$

$$D(\tau) = -B(\tau). \tag{3.11}$$

Finally, eq. (3.7b) simplifies to

$$D'(\tau) + A'(\tau) = 0,$$

which integrates to

$$D(\tau) = -A(\tau) + c_3.$$

Thus, all tangent fields given the Ansatz must be on the form

$$(\xi_1(\tau, y), \eta_1(\tau, y)) = (A(\tau) + (A(\tau) - c_3)y, (-A(\tau) + c_3)y). \tag{3.12}$$

Case of $n = 2$

When $n = 2$, $y^1 = y^{n-1}$. Equation (3.4) then separates into the system

$$y^0: \qquad C'(\tau) = 0 \tag{3.13a}$$

$$y^1: \qquad D'(\tau) = -2C(\tau) \tag{3.13b}$$

$$y^2: \qquad 2C'(\tau) + A'(\tau) - D(\tau) = -2D(\tau) \tag{3.13c}$$

$$y^3: \qquad 2D'(\tau) + B'(\tau) = 0 \tag{3.13d}$$

$$y^4: \qquad C'(\tau)A'(\tau) - D(\tau) - B(\tau) = 0 \tag{3.13e}$$

$$y^5: \qquad D'(\tau) + B'(\tau) = 0. \tag{3.13f}$$

Subtracting eq. (3.13f) from eq. (3.13d) gives

$$D'(\tau) = 0,$$

which integrates to

$$D(\tau) = c_1.$$

Thus eq. (3.13b) gives

$$C(\tau) = 0,$$

which renders eq. (3.13a) irrelevant. Equation (3.13c) simplifies to

$$A'(\tau) = -c_1,$$

which integrates to

$$A(\tau) = c_2 - c_1\tau.$$

Equation (3.13e) simplifies to

$$-c_1 - c_1 - B(\tau) = 0,$$

which means that

$$B(\tau) = -2c_1$$

and renders eq. (3.13f) irrelevant. Thus, all tangent fields must given the Ansatz be on the form

$$(\xi_2(\tau, y), \eta_2(\tau, y)) = (c_2 - c_1(\tau + 2y), c_1 y). \tag{3.14}$$

3.1.2 General form

To unify notation for any $n > 0$, eqs. (3.6), (3.12) and (3.14) can be summarized as

$$(\xi_n(\tau, y), \eta_n(\tau, y)) = (\tilde{c}_1 + \tilde{c}_2((1-n)\tau - ny), \tilde{c}_2 y), \tag{3.15}$$

where $\tilde{c}_1$ and $\tilde{c}_2$ are constants. For $n = 1$ this form can be achieved by specifying that $A(\tau)$ has a constant value and grouping the two resulting constants in the right way. This constriction on $A(\tau)$ when $n = 1$ also means that there are additional symmetries in the case $n = 1$ which are not symmetries for formulations with all other $n > 0$.

The aim of this section was to find a useful symmetry group. That is, a symmetry group that varies for different Hill coefficients n. The symmetry group in eq. (3.15) clearly varies in such a way. Just from looking at the problem, it was also determined that there is a symmetry group generated by $(\xi, \eta) = (1, 0)$ that does not vary with n. As this generator is linear in y, it is part of the generator in eq. (3.15). By separating the generator by the terms with $\tilde{c}_1$ and $\tilde{c}_2$, a basis for the vector space of symmetry groups on the form in eq. (3.15) can be established. One natural basis is

$$\begin{aligned} X_1 &= \partial_\tau \\ X_2 &= -((n-1)\tau + ny)\partial_\tau + y\partial_y, \end{aligned}$$

where X_1 generates the non-varying symmetry group observed. X_2 on the other hand generates symmetry groups varying with n, and can thus be used to distinguish between different Hill equations. As can be seen in [9], this fact can be used to select between Hill equations when given data generated by the equation with a specific value of n, even when other methods fail.

3.2 The Gompertz model

Since there are 3 different formulations of the Gompertz model, symmetries for each will be calculated separately.

3.2.1 The classical Gompertz model

For the classical Gompertz model, two parametrizations exist. As the success of the ansatz method does not hinge on the parametrization, the T_i-parametrization is chosen.

The ansatz

$$\begin{aligned} \xi &= f_1(t) + f_2(t)W \\ \eta &= f_3(t) + f_4(t)W \end{aligned}$$

is chosen, where f_i for $i = 1, 2, 3, 4$ are arbitrary functions in t. This results in the determining equation

$$\begin{aligned} &- W^2 k_G^2 f_2(t) e^{2T_i k_G} e^{-2k_G t} + W^2 k_G^2 f_2(t) e^{T_i k_G} e^{-k_G t} - \\ &\quad - W^2 k_G e^{T_i k_G} e^{-k_G t} f_2'(t) + W k_G^2 f_1(t) e^{T_i k_G} e^{-k_G t} - W k_G e^{T_i k_G} e^{-k_G t} f_1'(t) + \\ &\qquad + W f_4'(t) - k_G f_3(t) e^{T_i k_G} e^{-k_G t} + f_3'(t) = 0. \end{aligned}$$

Separating the system by powers of W, the ansatz determining equations are

$$\begin{aligned} W^2: &\quad k_G^2 f_2(t) e^{T_i k_G} e^{-k_G t} - k_G^2 f_2(t) e^{2T_i k_G} e^{-2k_G t} - k_G e^{T_i k_G} e^{-k_G t} f_2'(t) = 0 \\ W: &\quad k_G^2 f_1(t) e^{T_i k_G} e^{-k_G t} - k_G e^{T_i k_G} e^{-k_G t} f_1'(t) + f_4'(t) = 0 \\ 1: &\quad -k_G f_3(t) e^{T_i k_G} e^{-k_G t} + f_3'(t) = 0. \end{aligned}$$

This system of equations has solutions resulting in the general form for a tangent field corresponding to a symmetry being

$$\begin{aligned} \xi(t, W) &= W c_2 e^{\left(k_G t e^{k_G t} + e^{T_i k_G}\right) e^{-k_G t}} + c_1 e^{k_G t} + \frac{f_4(t) e^{-T_i k_G} e^{k_G t}}{k_G} \\ \eta(t, W) &= W f_4(t) + c_3 e^{-e^{T_i k_G} e^{-k_G t}}, \end{aligned}$$

where c_1, c_2, c_3 are arbitrary constants. Thus, by separating the tangent field into terms with independent arbitrary elements, the infinitesimal generators

$$\begin{aligned} X_{\mathrm{c},1} &= e^{k_G t} \partial_t \\ X_{\mathrm{c},2} &= W e^{k_G t + e^{T_i k_G} e^{-k_G t}} \partial_t \\ X_{\mathrm{c},3} &= e^{-e^{T_i k_G} e^{-k_G t}} \partial_W \\ X_{\mathrm{c},f} &= \frac{f(t) e^{-T_i k_G} e^{k_G t}}{k_G} \partial_t + W f(t) \partial_W \end{aligned}$$

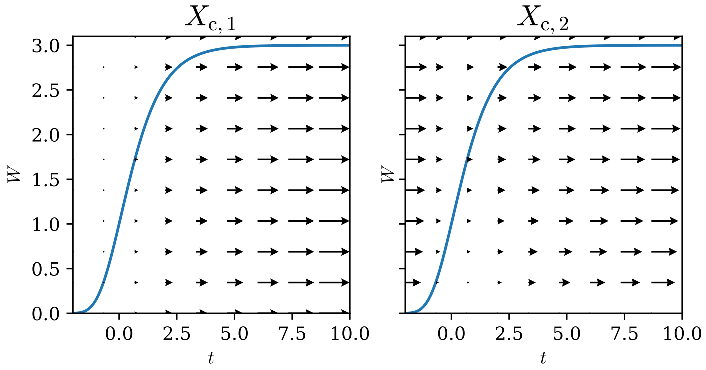

Figure 3.1: The vector field of generators $X_{c,1}$ and $X_{c,2}$ superimposed on a solution curve. The dt- and dW-components of the vector fields are shown on a $\log(1+x)$ scale.

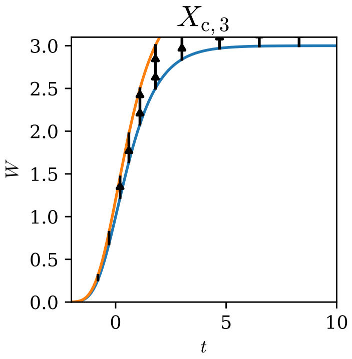

Figure 3.2: A representative transformation of the Lie group corresponding to the only non-trivial non-local symmetry generator of the classical Gompertz model found using an ansatz.

of Lie point symmetries of the autonomous Gompertz ODE (1.13) are found. The generator $X_{c,f}$ is easily shown to be trivial, and is therefore not very useful. Additionally, both $X_{c,1}$ and $X_{c,2}$ only generate local symmetries. This is due to their exponential growth in t for the ∂_t-term, which can be seen in fig. 3.1. A representative of the only remaining transformation group, corresponding to $X_{c,3}$, is shown in fig. 3.2.

3.2.2 The autonomous Gompertz model

The ansatz

$$\xi(t,W) = f_1(t) + f_2(t)\ln\left(\frac{W}{A}\right),$$

$$\eta(t,W) = f_3(t)W + f_4(t)\ln\left(\frac{W}{A}\right)W$$

can be taken, where f_i for $i = 1, 2, 3, 4$ are arbitrary functions in t. This results in the determining equation

$$\begin{aligned}
&f_3'(t)W + f_4'(t)\ln\left(\frac{W}{A}\right)W \\
&\quad + \left(f_3(t) + f_4(t)\left(1 + \ln\left(\frac{W}{A}\right)\right) - \left(f_1'(t) + f_2'(t)\ln\left(\frac{W}{A}\right)\right)\right) \cdot -k_G \ln\left(\frac{W}{A}\right)W \\
&\quad - \frac{f_2(t)}{W}\left(k_G \ln\left(\frac{W}{A}\right)W\right)^2 = \\
&\quad = \left(f_3(t)W + f_4(t)\ln\left(\frac{W}{A}\right)W\right) \cdot -k_G\left(1 + \ln\left(\frac{W}{A}\right)\right)
\end{aligned}$$

which can be reduced to

$$\begin{aligned}
&f_3'(t)W + (f_4'(t) + k_G f_1'(t))\ln\left(\frac{W}{A}\right)W + (f_2'(t) - k_G f_2(t))k_G \ln\left(\frac{W}{A}\right)^2 W = \\
&\quad = -k_G f_3(t)W
\end{aligned}$$

By separating the equation based on powers of $\ln\left(\frac{W}{A}\right)$, the system

$$W : \qquad f_3'(t) = -k_G f_3(t) \tag{3.17a}$$

$$\ln\left(\frac{W}{A}\right)W : \qquad f_4'(t) + k_G f_1'(t) = 0 \tag{3.17b}$$

$$k_G \ln\left(\frac{W}{A}\right)^2 W : \qquad f_2'(t) - k_G f_2(t) = 0 \tag{3.17c}$$

can be acquired. This system of equations has the solution

$$\begin{aligned}
\xi(t, W) &= f_1(t) + c_1 e^{k_G t}\ln\left(\frac{W}{A}\right), \\
\eta(t, W) &= c_2 e^{-k_G t}W + (c_3 - k_G f_1(t))\ln\left(\frac{W}{A}\right)W,
\end{aligned}$$

where c_1, c_2 and c_3 are arbitrary constants. Thus, by separating the tangent field into terms with independent arbitrary elements, the infinitesimal generators

$$\begin{aligned}
X_{\mathrm{a},1} &= e^{k_G t}\ln\left(\frac{W}{A}\right)\partial_t \\
X_{\mathrm{a},2} &= e^{-k_G t}W\partial_W \\
X_{\mathrm{a},3} &= \ln\left(\frac{W}{A}\right)W\partial_W \\
X_{\mathrm{a},f} &= f(t)\partial_t - k_G f(t)\ln\left(\frac{W}{A}\right)W\partial_W
\end{aligned}$$

of Lie point symmetries of the autonomous Gompertz ODE (1.15) are found. The corresponding transformations can be seen in fig. 3.3.

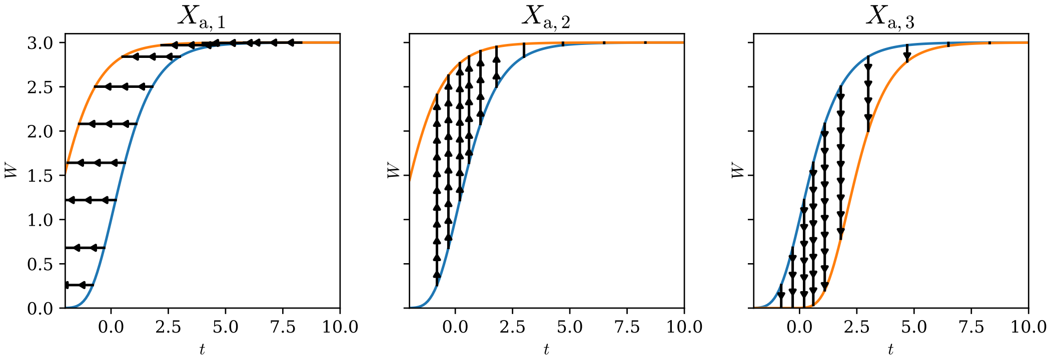

Figure 3.3: Representative transformations of the Lie groups corresponding to symmetry generators of the autonomous Gompertz model found using an ansatz.

3.2.3 The system Gompertz model

As models and ansätze grow in size, the determining equations grow. This becomes particularly prominent for systems of ODE:s. For this reason, the calculations for the remaining models in this chapter have been made using computer algebra using code outlined in appendix A.

Similarly to the classical Gompertz model, the ansatz

$$\begin{aligned}\xi(t,W,G)&=f_1(t)+f_2(t)W+f_3(t)G\\ \eta^1(t,W,G)&=f_4(t)+f_5(t)W+f_6(t)G\\ \eta^2(t,W,G)&=f_7(t)+f_8(t)W+f_9(t)G,\end{aligned}$$

where f_i are arbitrary functions in t, is used. The two determining equations can be decomposed in W and G, resulting in 15 algebraic and ordinary differential equations. By first solving the algebraic equations, followed by the differential for the arbitrary functions f_i, their form can be determined resulting in the general form

$$\begin{aligned}\xi(t,W,G)&=Gc_3e^{k_Gt}+c_1-\frac{c_2e^{k_Gt}}{k_G}\\ \eta^1(t,W,G)&=Wc_4-\frac{Wc_5e^{-k_Gt}}{k_G}\\ \eta^2(t,W,G)&=Gc_2e^{k_Gt}+c_5e^{-k_Gt}.\end{aligned}$$

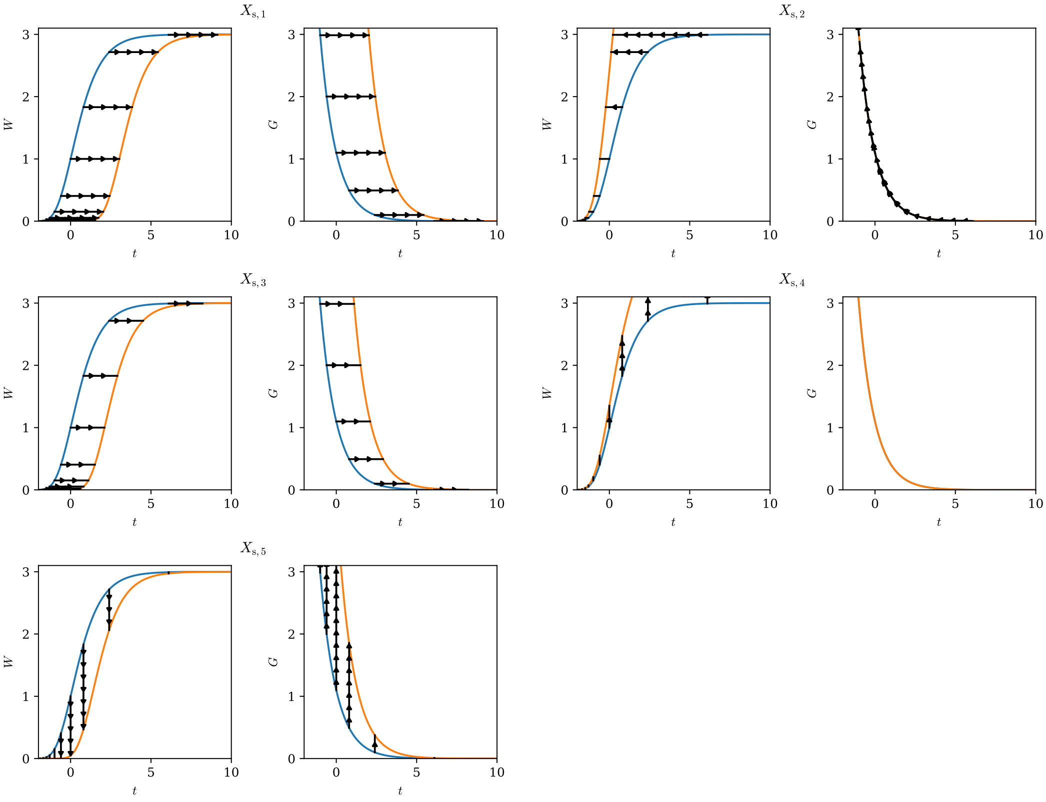

Figure 3.4: Representative transformations of the Lie groups corresponding to symmetry generators of the system Gompertz model found using an ansatz.

Decomposition in arbitrary constants result in the basis

$$\begin{aligned}
X_{\mathrm{s},1} &= \partial_t\\
X_{\mathrm{s},2} &= -\frac{e^{k_G t}}{k_G}\partial_t + G e^{k_G t}\partial_G\\
X_{\mathrm{s},3} &= G e^{k_G t}\partial_t\\
X_{\mathrm{s},4} &= W\partial_W\\
X_{\mathrm{s},5} &= -\frac{W e^{-k_G t}}{k_G}\partial_W + e^{-k_G t}\partial_G.
\end{aligned}$$

The corresponding transformations can be seen in fig. 3.4.

3.3 The Lotka–Volterra model

The Lotka–Volterra predator-prey model formulated in eqs. (1.17) has a right hand side formulated as second order polynomial in the two states N and P. A good starting point for ansätze is therefore polynomials, and arbitrary third degree polynomials in t, N and P are chosen. The ansatz will thus have the form

$$\begin{aligned}
\xi &= c_{1,1} + c_{1,2}t + c_{1,3}N + c_{1,4}P + c_{1,5}t^2 + c_{1,6}tN + c_{1,7}N^2 + c_{1,8}tP + && \text{(3.18a)}\\
&\quad + c_{1,9}NP + c_{1,10}P^2 + c_{1,11}t^3 + c_{1,12}t^2N + c_{1,13}tN^2 + c_{1,14}N^3 + && \text{(3.18b)}\\
&\quad + c_{1,15}t^2P + c_{1,16}tNP + c_{1,17}N^2P + c_{1,18}tP^2 + c_{1,19}NP^2 + c_{1,20}P^3 && \text{(3.18c)}\\
\eta^1 &= c_{2,1} + c_{2,2}t + c_{2,3}N + c_{2,4}P + c_{2,5}t^2 + c_{2,6}tN + c_{2,7}N^2 + c_{2,8}tP + && \text{(3.18d)}\\
&\quad + c_{2,9}NP + c_{2,10}P^2 + c_{2,11}t^3 + c_{2,12}t^2N + c_{2,13}tN^2 + c_{2,14}N^3 + && \text{(3.18e)}\\
&\quad + c_{2,15}t^2P + c_{2,16}tNP + c_{2,17}N^2P + c_{2,18}tP^2 + c_{2,19}NP^2 + c_{2,20}P^3 && \text{(3.18f)}\\
\eta^2 &= c_{3,1} + c_{3,2}t + c_{3,3}N + c_{3,4}P + c_{3,5}t^2 + c_{3,6}tN + c_{3,7}N^2 + c_{3,8}tP + && \text{(3.18g)}\\
&\quad + c_{3,9}NP + c_{3,10}P^2 + c_{3,11}t^3 + c_{3,12}t^2N + c_{3,13}tN^2 + c_{3,14}N^3 + && \text{(3.18h)}\\
&\quad + c_{3,15}t^2P + c_{3,16}tNP + c_{3,17}N^2P + c_{3,18}tP^2 + c_{3,19}NP^2 + c_{3,20}P^3, && \text{(3.18i)}
\end{aligned}$$

where $c_{i,j}$ are arbitrary constants. The linearized symmetry condition will thus consist of two equations, each of which must hold for arbitrary t, N and P. The two equations can thus be decomposed into 98 linear equations in the arbitrary constants $c_{i,j}$. The solution to this overdetermined system of equations gives that any symmetry generator on the form of the ansatz can be written as a linear combination of the generators

$$\begin{aligned}
X_1 &= \partial_t\\
X_2 &= \frac{-bNP + aN}{c}\partial_N + \frac{cNP - dP}{c}\partial_P\\
X_3 &= \frac{t}{c}\partial_t + \frac{-btNP + atN}{c}\partial_N + \frac{ctNP - dtP}{c}\partial_P\\
X_4 &= \frac{N}{c}\partial_t + \frac{-bcN^2P + acN^2 - bdNP + adN}{c^2}\partial_N + \frac{c^2N^2P - d^2P}{c^2}\partial_P\\
X_5 &= \frac{P}{c}\partial_t + \frac{-bNP^2 + aNP}{c}\partial_N + \frac{cNP^2 - dP^2}{c}\partial_P
\end{aligned}$$

3.4 The Yildirim–Mackey lactose operon model

Since the lactose operon model formulated in eqs. (1.18) is significantly larger than all other models studied, the performance of the computer algebra system places restrictions on the ansätze viable to test. Additionally, the decomposition of the linearized symmetry condition becomes less straight forward as the right hand side of the lactose operon model contains both fractions and arbitrary powers of the state A.

A simple ansatz is that the infinitesimal generator is linear in time and the states, formulated as

$$\begin{aligned}
\xi &= c_{1,1} + c_{1,2}t + c_{1,3}M + c_{1,4}B + c_{1,5}L + c_{1,6}A + c_{1,7}P \\
\eta^1 &= c_{2,1} + c_{2,2}t + c_{2,3}M + c_{2,4}B + c_{2,5}L + c_{2,6}A + c_{2,7}P \\
\eta^2 &= c_{3,1} + c_{3,2}t + c_{3,3}M + c_{3,4}B + c_{3,5}L + c_{3,6}A + c_{3,7}P \\
\eta^3 &= c_{4,1} + c_{4,2}t + c_{4,3}M + c_{4,4}B + c_{4,5}L + c_{4,6}A + c_{4,7}P \\
\eta^4 &= c_{5,1} + c_{5,2}t + c_{5,3}M + c_{5,4}B + c_{5,5}L + c_{5,6}A + c_{5,7}P \\
\eta^5 &= c_{6,1} + c_{6,2}t + c_{6,3}M + c_{6,4}B + c_{6,5}L + c_{6,6}A + c_{6,7}P,
\end{aligned}$$

where $c_{i,j}$ are arbitrary constants. The linearized symmetry condition will thus consist of 5 equations, which will consist of sums of fractional expressions in the states. To decompose the system, the sums in all equations are rewritten with a common denominator. Additionally, since the power A^n appear in some of the equations, and all equations sought should hold for an arbitrary n, the numerator of the equations written with common denominators is decomposed in t, M, B, L, A, P and A^n. The decomposition results in 1901 equations, all linear in the arbitrary constants $c_{i,j}$. The solution to the overdetermined system of equations gives that the only symmetry generator on the form of the ansatz is the manifest generator

$$X_1 = \partial_t.$$

Chapter 4

Finding symmetries using parameter independence

In chapter 3 the traditional approach of using ansätze to find symmetries of first order ODE:s was used. There are two main problems with using ansätze.

Firstly, there is a lack of systematics in the process. There are algorithms that have high success rates at finding symmetries of first order ODE:s that use a heuristic approach [3, 4]. These methods are however not aimed at finding as many symmetries as possible, but rather finding enough symmetries to integrate the system. If the goal is to draw new biological conclusions from the symmetries, this is insufficient, as the algorithm is considered equally good if it finds the time invariance generated by ∂_t as if it finds a more biologically complex symmetry. Thus such schemes would have to be reevaluated, focusing on metrics such as the number of symmetries, and run on collections of ODE:s on forms common in biology.

Secondly, using ansätze to find symmetries gives information about systems unreliably. Unless the ansatz can be tied to some biological concept independently of the system studied, solving the symmetry conditions using an ansatz only contributes to the knowledge about the systems if new symmetries are found. Any negative information about which symmetries exist will be hard enough to interpret that it will be discarded in most cases.

In this chapter, a new approach to making the linearized symmetry condition viable to solve for first order ODE:s is presented and used. The central concept of the method is finding symmetries that are independent of one or more parameters of an ODE model. It is heavily inspired by methods used in group classification introduced by Ovsiannikov [31]. The group classification problem centers around models that contain parameters which are not limited to being constants, but instead can be any arbitrary function in the states of the model. The general biological models described in chapter 1 are special cases of such models, where the parameters are limited to being constants. This chapter has a description of the method of parameter independence for such models, followed by application of the method to the models under study.

4.1 The parameter independence method

Consider a system of first order ODE:s

$$\frac{d\boldsymbol{u}}{dt} = \boldsymbol{\omega}(t, \boldsymbol{u}; \boldsymbol{\theta}) \tag{4.1}$$

with states $\boldsymbol{u} = (u^1, \ldots, u^s)$, parametrized by constant parameters $\boldsymbol{\theta} = (\theta^1, \ldots, \theta^m)$. In traditional symmetry calculations, the ODE (4.1) is seen as a single equation, where the parameters $\boldsymbol{\theta}$ have unknown but fixed values. Any symmetry found through calculations is a symmetry of the equation defined by that specific set of parameters $\boldsymbol{\theta}$, which shows itself in symmetry generators themselves containing the parameters. In contrast, an ODE used in modeling is often seen as a collection of models. Some parameters might be fixed at the same value in all valid uses of the model, but most parameters are intended to vary over different use cases. To take biochemistry as an example, while some parameters might indicate the reaction speed between two chemicals (which is seen as fixed), most parameters are intended to vary between conditions the cells are in or between individuals in a cell population.

When interpreting symmetries, the distinction between symmetries for specific instances of the model and symmetries of certain families of the model becomes important. While there are no known methods for finding all the symmetries of a specific system of first order ODE:s, it is possible to find all symmetries common to a family parametrized by one of the parameters $\theta^1, \ldots, \theta^m$. Without loss of generality, the one-parameter family of functions

$$\Omega = \Big\{ \boldsymbol{u}_t - \boldsymbol{\omega}(t, \boldsymbol{u}; \boldsymbol{\theta}) : \quad \theta^1 \in S \subseteq \mathbb{R} \Big\}$$

with fixed parameters $\theta^2, \ldots, \theta^m$ can be considered. Call a Lie point symmetry with infinitesimal generator $X = \xi(x, \boldsymbol{u})\partial_t + \boldsymbol{\eta}(x, \boldsymbol{u}) \cdot \partial_{\boldsymbol{u}}$ a symmetry of the family of ODE:s defined by

$$\boldsymbol{\Delta}(\underset{1}{z}) = 0, \quad \boldsymbol{\Delta} \in \Omega$$

if

$$\underset{1}{X}\Big(\boldsymbol{\Delta}(\underset{1}{z})\Big)\Big|_{\boldsymbol{\Delta}(\underset{1}{z})=0} = 0, \quad \forall \boldsymbol{\Delta} \in \Omega.$$

Thus, an infinitesimal generator X of a family of ODE:s defined by Ω can not have any dependence on θ^1. Evaluating the linearized symmetry condition, it takes the form

$$\eta_t - \omega^k \xi_t + \sum_{i=1}^{s} \omega^i \eta^k_{u^i} - \sum_{i=1}^{s} \omega^k \omega^i \xi_{u^i} - \omega^k_t \xi - \sum_{i=1}^{s} \omega^k_{u^i} \eta^i = 0, \quad \forall k = 1, \ldots, s.$$

Since the parameter θ^1 appears in at least one function ω^j, and every equation of the linearized symmetry condition includes any ω^j at least once, decomposition of the equations in θ^1 results in a set of at least $2s + 1$ equations (taking the $\omega^k \omega^k$-term for equation $k = j$ into account), that will henceforth be called the parameter independence determining equations. Just like the determining equations for higher order ODE:s, the parameter independence determining equations create a solvable system of PDE:s, whose solution is the most general form of a symmetry generator for the problem.

This method addresses both previously mentioned weaknesses of using ansätze. Firstly, the process of finding symmetries by parameter independence is highly systematic. The method can be used for all parameters of a model, at which point calculations will have revealed all Lie point symmetries independent of one or more of the parameters of the model. This creates a clear stopping point for calculations. Secondly, calculations resulting in no parameter independent symmetries being found can still be informative to the modeler since most parameters tend to be connected to some natural concept.

4.2 The Gompertz model

To reiterate, the Gompertz models are

$$\text{Classical,} \quad T_i: \qquad \frac{dW}{dt} = k_G e^{-k_G(t-T_i)} W(t) \tag{4.2}$$

$$\text{Classical,} \quad W_0: \qquad \frac{dW}{dt} = k_G \ln\left(\frac{W_0}{A}\right) e^{-k_G t} W(t) \tag{4.3}$$

$$\text{Autonomous,} \quad T_i \text{ and } W_0: \qquad \frac{dW}{dt} = -k_G \ln\left(\frac{W(t)}{A}\right) W(t) \tag{4.4}$$

$$\text{System,} \quad T_i \text{ and } W_0: \qquad \frac{dW}{dt} = G(t)W(t) \tag{4.5a}$$

$$\frac{dG}{dt} = -k_G G(t). \tag{4.5b}$$

As was seen in chapter 3, several symmetries exist for each of the models. Some of these symmetries were independent of one or more parameters, and should therefore be found using the parameter independence method. It is however of interest to see if any symmetries not found using the specific ansätze used in chapter 3 can be found using the parameter independence method.

4.2.1 The classical Gompertz model

For the classical Gompertz model, two different parametrizations exist. For the purposes of the parameter independence method, either of these parametrizations may be used since the parameters T_i and W_0 only depend on each other and the parameter k_G, but neither the time t nor the state W. The T_i-parametrization will be used in these calculations.

The linearized symmetry condition (2.8) is for the classical T_i-parametrized Gompertz model

$$\begin{aligned} &\eta_t + k_G e^{-k_G(t-T_i)} W(\eta_W - \xi_t) - (k_G)^2 e^{-2k_G(t-T_i)} W^2 \xi_W + \\ &\quad + (k_G)^2 e^{-k_G(t-T_i)} W \xi - k_G e^{-k_G(t-T_i)} \eta = 0. \end{aligned} \tag{4.6}$$

For a generator (ξ, η) to be independent of a parameter, eq. (4.6) is decomposed by functionally independent coefficients of that parameter.

k_G-independent symmetries

Decomposition of eq. (4.6) in k_G gives the parameter independence determining equations

$$
\begin{aligned}
1 &: & \eta_t &= 0 && \text{(4.7a)}\\
k_G e^{-k_G(t-T_i)} &: & W(\eta_W - \xi_t) - \eta &= 0 && \text{(4.7b)}\\
(k_G)^2 e^{-k_G(t-T_i)} &: & W\xi &= 0 && \text{(4.7c)}\\
(k_G)^2 e^{-2k_G(t-T_i)} &: & W^2\xi_W &= 0. && \text{(4.7d)}
\end{aligned}
$$

From eq. (4.7c) it is clear that

$$\xi \equiv 0,$$

and hence eq. (4.7d) must also hold. From eq. (4.7a) it is clear that

$$\eta = \eta(W)$$

is a function only in W. This leaves eq. (4.7b) that simplifies into the ODE

$$W\eta_W - \eta = 0$$

with the general solution

$$\eta = c_1 W,$$

where c_1 is an arbitrary constant. Thus any k_G-independent symmetry generator of the classical Gompertz model (4.2) must have the form

$$
\begin{aligned}
\xi &= 0\\
\eta &= c_1 W,
\end{aligned}
$$

which is spanned by the generator basis

$$X_{\mathrm{c},4} = W\partial_W.$$

T_i-independent symmetries

Decomposition of eq. (4.6) in T_i gives the parameter independence determining equations

$$
\begin{aligned}
1 &: & \eta_t &= 0 && \text{(4.8a)}\\
e^{k_G T_i} &: & k_G e^{-k_G t} W(\eta_W - \xi_t) + (k_G)^2 e^{-k_G t} W\xi - k_G e^{-k_G t}\eta &= 0 && \text{(4.8b)}\\
e^{2k_G T_i} &: & -(k_G)^2 e^{-2k_G t} W^2 \xi_W &= 0 && \text{(4.8c)}
\end{aligned}
$$

From eqs. (4.8a) and (4.8c) it is clear that

$$\begin{aligned}\eta &= \eta(W)\\ \xi &= \xi(t)\end{aligned}$$

respectively. Dividing eq. (4.8b) by $k_G e^{-k_G t}$ gives

$$W(\eta_W - \xi_t) + k_G W \xi - \eta = 0, \tag{4.9}$$

which can be rewritten as

$$k_G \xi - \xi_t = \frac{\eta}{W} - \eta_W. \tag{4.10}$$

Separation of variables gives that

$$k_G \xi - \xi_t = c_1 = \frac{\eta}{W} - \eta_W \tag{4.11}$$

for some constant c_1, where both the left and right hand sides are straight forward to solve since they are only dependent in one variable each. Thus any T_i-independent symmetry generator of the classical Gompertz model (4.2) must have the form

$$\begin{aligned}\xi &= \frac{c_1}{k_G} + c_2 e^{k_G t}\\ \eta &= -c_1 W \ln(W) + c_3 W,\end{aligned}$$

which is spanned by the generator basis

$$\begin{aligned}X_{\mathrm{c},1} &= e^{k_G t}\partial_t\\ X_{\mathrm{c},4} &= W\partial_W\\ X_{\mathrm{c},5} &= \partial_t - k_G W \ln(W)\partial_W.\end{aligned}$$

All of the found generators

The basis of all the generators found by the parameter independence method for the classical Gompertz model are

$$\begin{aligned}X_{\mathrm{c},1} &= e^{k_G t}\partial_t\\ X_{\mathrm{c},4} &= W\partial_W\\ X_{\mathrm{c},5} &= \partial_t - k_G W \ln(W)\partial_W.\end{aligned}$$

The corresponding transformations can be seen in fig. 4.1.

4.2.2 The autonomous Gompertz model

For the autonomous Gompertz model there is only one parametrization of interest. The linearized symmetry condition (2.8) is for the autonomous Gompertz model

$$\begin{aligned}&\eta_t - k_G \ln\left(\frac{W}{A}\right) W(\eta_W - \xi_t) - (k_G)^2 \left(\ln\left(\frac{W(t)}{A}\right)\right)^2 W^2 \xi_W +\\ &+ k_G\left(\ln\left(\frac{W}{A}\right) + 1\right)\eta = 0.\end{aligned} \tag{4.12}$$

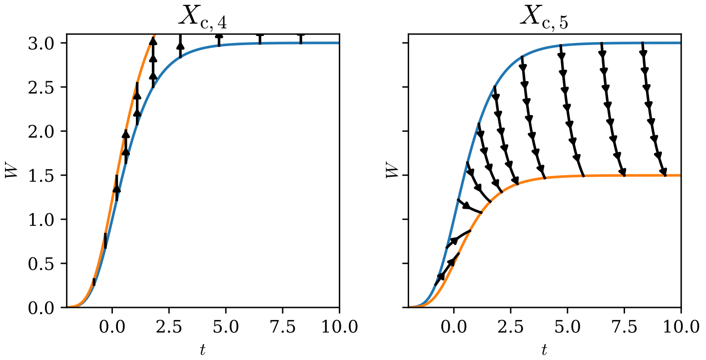

Figure 4.1: Representative transformations of the Lie groups corresponding to symmetry generators of the classical Gompertz model found using the parameter independence method. For the generator $X_{\mathrm{c},1}$, a vector field is instead shown since the symmetry generator only acts locally. The dt– and dW–components of the vector field is shown on a $\log(1+x)$ scale.

k_G-independent symmetries

Decomposition of eq. (4.12) in k_G gives the parameter independence determining equations

$$1: \qquad \eta_t = 0 \tag{4.13a}$$

$$k_G: \qquad -\ln\left(\frac{W}{A}\right)W(\eta_W - \xi_t) + \left(\ln\left(\frac{W}{A}\right)+1\right)\eta = 0 \tag{4.13b}$$

$$(k_G)^2: \qquad -\left(\ln\left(\frac{W(t)}{A}\right)\right)^2 W^2 \xi_W = 0. \tag{4.13c}$$

From eqs. (4.13a) and (4.13c)

$$\eta = \eta(W)$$
$$\xi = \xi(t).$$

Hence, since the only source of time dependence in eq. (4.13b) is ξ_t,

$$\xi_t = c_1$$

where c_1 is an arbitrary constant, and thus

$$\xi = c_1 t + c_2$$

for an additional arbitrary constant c_2. Equation (4.13b) can thus be rewritten as

$$\eta_W - \frac{\ln\left(\frac{W}{A}\right)+1}{\ln\left(\frac{W}{A}\right)W}\eta - c_1 = 0,$$

which is a scalar first order ODE with the solution

$$\eta = c_1 \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) \ln\left(\frac{W}{A}\right) W + c_3 \ln\left(\frac{W}{A}\right) W.$$

Thus any k_G-independent symmetry generator of the autonomous Gompertz model (4.4) must have the form

$$\begin{aligned} \xi &= c_2 + c_1 t \\ \eta &= c_1 \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) \ln\left(\frac{W}{A}\right) W + c_3 \ln\left(\frac{W}{A}\right) W, \end{aligned}$$

which is spanned by the generator basis

$$\begin{aligned} X_{\mathrm{a},3} &= \ln\left(\frac{W}{A}\right) W \partial_W \\ X_{\mathrm{a},4} &= \partial_t \\ X_{\mathrm{a},5} &= t\partial_t + \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) \ln\left(\frac{W}{A}\right) W \partial_W. \end{aligned}$$

A-independent symmetries

Decomposition of eq. (4.12) in A gives the parameter independence determining equations

$$1: \qquad \eta_t + k_G \eta = 0 \tag{4.14a}$$

$$\ln\left(\frac{W}{A}\right): \qquad -k_G W(\eta_W - \xi_t) + k_G \eta = 0 \tag{4.14b}$$

$$\left(\ln\left(\frac{W}{A}\right)\right)^2: \qquad -(k_G)^2 W^2 \xi_W = 0. \tag{4.14c}$$

From eq. (4.14c)

$$\xi = \xi(t).$$

Since η (and thus its derivative) are the only unknown sources of W-dependence in eq. (4.14b),

$$\eta_W - \frac{1}{W}\eta = \xi_t(t)$$

must hold. Integration in W gives

$$\eta = \ln(W) W \xi_t(t) + W f(t)$$

for some arbitrary function f in time. Inserting this result in eq. (4.14a) gives

$$\ln(W) W \xi_{tt} + W f_t + k_G \ln(W) W \xi_t + k_G W f = 0$$

which can be decomposed by W into

$$\begin{aligned} \xi_{tt} + k_G \xi_t &= 0 \\ f_t + k_G f &= 0 \end{aligned}$$

with solutions

$$\begin{aligned} \xi &= -c_1 \frac{1}{k_G} e^{-k_G t} + c_2 \\ f &= c_3 e^{-k_G t}. \end{aligned}$$

Thus any A-independent symmetry generator of the autonomous Gompertz model (4.4) must have the form

$$\begin{aligned} \xi &= -c_1 \frac{1}{k_G} e^{-k_G t} + c_2 \\ \eta &= c_1 e^{-k_G t} \ln(W) W + c_3 e^{-k_G t} W, \end{aligned}$$

which is spanned by the generator basis

$$\begin{aligned} X_{\mathrm{a},2} &= e^{-k_G t} W \partial_W \\ X_{\mathrm{a},4} &= \partial_t \\ X_{\mathrm{a},6} &= e^{-k_G t} \partial_t - k_G e^{-k_G t} \ln(W) W \partial_W . \end{aligned}$$

All found generators

The basis of all the generators found by the parameter independence method for the autonomous Gompertz model are

$$\begin{aligned} X_{\mathrm{a},2} &= e^{-k_G t} W \partial_W \\ X_{\mathrm{a},3} &= \ln\left(\frac{W}{A}\right) W \partial_W \\ X_{\mathrm{a},4} &= \partial_t \\ X_{\mathrm{a},5} &= t\partial_t + \ln\left(\left| \ln\left(\frac{W}{A}\right) \right| \right) \ln\left(\frac{W}{A}\right) W \partial_W \\ X_{\mathrm{a},6} &= e^{-k_G t} \partial_t - k_G e^{-k_G t} \ln(W) W \partial_W . \end{aligned}$$

The corresponding transformations can be seen in fig. 4.2.

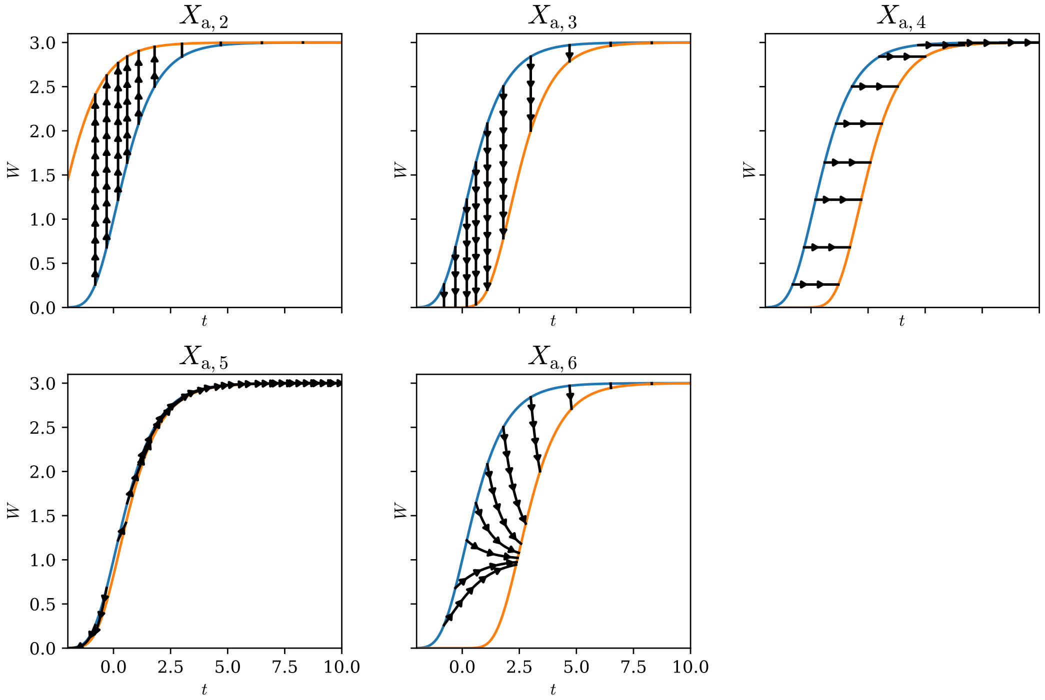

Figure 4.2: Representative transformations of the Lie groups corresponding to symmetry generators of the autonomous Gompertz model found using the parameter independence method.

4.2.3 The system Gompertz model

For the system Gompertz model there is also only one parametrization of interest. The linearized symmetry condition (2.8) is for the system Gompertz model

$$\begin{split}\eta^1_t + WG\Big(\eta^1_W - \xi_t\Big) - k_G G\eta^1_G - W^2G^2\xi_W + \\ + k_G W G^2 \xi_G - G\eta^1 - W\eta^2 = 0\end{split}\tag{4.15a}$$

$$\begin{split}\eta^2_t - k_G G\Big(\eta^2_G - \xi_t\Big) + WG\eta^2_W + k_G W G^2 \xi_W - \\ -(k_G)^2 G^2 \xi_G + k_G \eta^2 = 0.\end{split}\tag{4.15b}$$

k_G-independent symmetries

Decomposition of eqs. (4.15) in k_G gives the parameter independence determining equations

$$\text{(4.15a), } 1: \qquad \eta^1_t + WG\Big(\eta^1_W - \xi_t\Big) - W^2G^2\xi_W - G\eta^1 - W\eta^2 = 0 \tag{4.16a}$$

$$\text{(4.15a), } k_G: \qquad -G\eta^1_G + WG^2\xi_G = 0 \tag{4.16b}$$

$$\text{(4.15b), } 1: \qquad \eta^2_t + WG\eta^2_W = 0. \tag{4.16c}$$

$$\text{(4.15b), } k_G: \qquad -G\Big(\eta^2_G - \xi_t\Big) + WG^2\xi_W + \eta^2 = 0. \tag{4.16d}$$

$$\text{(4.15b), } (k_G)^2: \qquad -G^2\xi_G = 0. \tag{4.16e}$$

From eq. (4.16e) it is clear that

$$\xi = \xi(t, W), \tag{4.17}$$

and thus from eq. (4.16b)

$$\eta^1 = \eta^1(t, W). \tag{4.18}$$

From eq. (4.16a)

$$\eta^2 = \frac{1}{W}\eta^1_t + G\Big(\eta^1_W - \xi_t - \frac{1}{W}\eta^1\Big) - WG^2\xi_W,$$

and thus eq. (4.16d) can be written as

$$\frac{1}{W}\eta^1_t + G\xi_t + 2G^2W\xi_W = 0. \tag{4.19}$$

Since both ξ and η^1 are not functions in G, eq. (4.19) can be decomposed in G giving

$$\begin{aligned}\xi_t &= 0\\ \xi_W &= 0\\ \eta^1_t &= 0.\end{aligned}$$

Thus

$$\begin{aligned} \xi &= c_1 \\ \eta^1 &= \eta^1(W) \\ \eta^2 &= G\Big(\eta^1_W(W) - \frac{1}{W}\eta^1(W)\Big), \end{aligned}$$

where c_1 is an arbitrary constant, and eq. (4.16c) reduces to

$$WG^2\Big(\eta^1_W - \frac{1}{W}\eta^1\Big)_W = 0.$$

Thus the ODE

$$\eta^1_W - \frac{1}{W}\eta^1 = c_2$$

must hold for an arbitrary constant c_2, which has the general solution

$$\eta^1 = c_2 \ln(W)W + c_3 W.$$

Thus any k_G-independent symmetry generator of the system Gompertz model (4.5) must have the form

$$\begin{aligned} \xi &= c_1 \\ \eta^1 &= c_2 \ln(W)W + c_3 W \\ \eta^2 &= c_2 G \end{aligned}$$

which is spanned by the generator basis

$$\begin{aligned} X_{\mathrm{s},1} &= \partial_t \\ X_{\mathrm{s},4} &= W\partial_W \\ X_{\mathrm{s},6} &= \ln(W)W\partial_W + G\partial_G. \end{aligned}$$

The corresponding transformations can be seen in fig. 4.3.

4.3 The Lotka–Volterra model

The linearized symmetry condition 2.3.2 is for the Lotka–Volterra model

$$\begin{aligned} &\eta^1_t + (aN - bN)\Big(\eta^1_N - \xi_t\Big) + (cNP - dP)\eta^1_P - (aN - bNP)^2\xi_N - \\ &\quad - (aN - bNP)(cNP - dP)\xi_P - (a - bP)\eta^1 + bN\eta^2 = 0 \end{aligned} \tag{4.20a}$$

$$\begin{aligned} &\eta^2_t + (aN - bNP)\eta^2_N + (cNP - dP)\Big(\eta^2_P - \xi_t\Big) - \\ &\quad - (aN - bNP)(cNP - dP)\xi_N - (cNP - dP)^2\xi_P - cP\eta^1 - \\ &\quad - (cN - d)\eta^2 = 0. \end{aligned} \tag{4.20b}$$

The only symmetry found in chapter 3 independent in any parameter is ∂_t. Thus the parameter independence method should find that generator, and if any new symmetry generators are found they will be new.

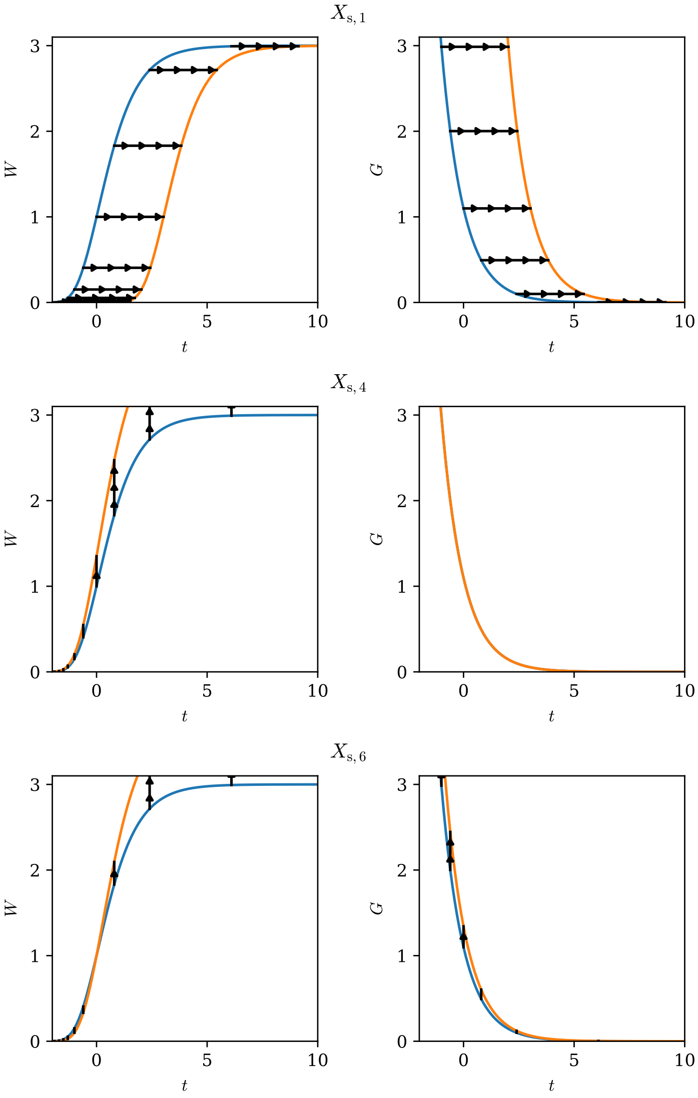

Figure 4.3: Representative transformations of the Lie groups corresponding to symmetry generators of the system Gompertz model found using the parameter independence method.

a-independent symmetries

Decomposition of eqs. (4.20) in a gives the parameter independence determining equations

$$
\begin{aligned}
\frac{dN}{dt}, 1: \quad & -N^2P^2b^2\xi_N - NPb\eta^1_N + NPb\xi_t + Nb\eta^2 + Pb\eta^1 + && \text{(4.21a)}\\
& +(NPc - Pd)\eta^1_P + \Big(N^2P^2bc - NP^2bd\Big)\xi_P + \eta^1_t = 0 && \text{(4.21b)}\\
\frac{dN}{dt}, a: \quad & 2N^2Pb\xi_N + N\eta^1_N - N\xi_t + \Big(-N^2Pc + NPd\Big)\xi_P - && \text{(4.21c)}\\
& -\eta^1 = 0 && \text{(4.21d)}\\
\frac{dN}{dt}, a^2: \quad & -N^2\xi_N = 0 && \text{(4.21e)}\\
\frac{dP}{dt}, 1: \quad & -NPb\eta^2_N - Pc\eta^1 + (-Nc + d)\eta^2 + && \text{(4.21f)}\\
& +(-NPc + Pd)\xi_t + (NPc - Pd)\eta^2_P + && \text{(4.21g)}\\
& +\Big(N^2P^2bc - NP^2bd\Big)\xi_N + && \text{(4.21h)}\\
& +\Big(-N^2P^2c^2 + 2NP^2cd - P^2d^2\Big)\xi_P + \eta^2_t = 0 && \text{(4.21i)}\\
\frac{dP}{dt}, a: \quad & N\eta^2_N + \Big(-N^2Pc + NPd\Big)\xi_N = 0. && \text{(4.21j)}
\end{aligned}
$$

From eqs. (4.21e) and (4.21j) it is clear that

$$
\begin{aligned}
\eta^2 &= \eta^2(t, P) && \text{(4.22a)}\\
\xi &= \xi(t, P), && \text{(4.22b)}
\end{aligned}
$$

and thus eq. (4.21i) can be written as

$$
\begin{aligned}
\eta^1 = \Big(-N + \frac{d}{c}\Big)\xi_t + \Big(N - \frac{d}{c}\Big)\eta^2_P + \Big(-\frac{N}{P} + \frac{d}{Pc}\Big)\eta^2 + \\
+ \left(-N^2Pc + 2NPd - \frac{Pd^2}{c}\right)\xi_P + \frac{\eta^2_t}{Pc}.
\end{aligned}
$$

Since neither ξ nor η^2 depends on N, and η^1 thus only depends explicitly on N, the remaining parameter independence determining equations (4.21b) and (4.21d) can be decomposed further in N resulting in the equations

$$-2Pc\xi_P = 0 \tag{4.23a}$$

$$Pd\xi_P - \xi_t = 0 \tag{4.23b}$$

$$\frac{Pd^2\xi_P}{c} + \frac{d\eta^2_P}{c} - \frac{d\xi_t}{c} - \frac{d\eta^2}{Pc} - \frac{\eta^2_t}{Pc} = 0 \tag{4.23c}$$

$$-P^2c^2\xi_{PP} - Pc^2\xi_P = 0 \tag{4.23d}$$

$$3P^2cd\xi_{PP} + Pc\eta^2_{PP} - 2Pc\xi_{Pt} - c\eta^2_P + \left(2P^2bc + 3Pcd\right)\xi_P + \frac{c\eta^2}{P} = 0 \tag{4.23e}$$

$$\begin{aligned} -3P^2d^2\xi_{PP} + Pb\xi_t - 2Pd\eta^2_{PP} + 4Pd\xi_{Pt} + 2d\eta^2_P + \left(b - \frac{2d}{P}\right)\eta^2 + \\ + \left(-P^2bd - 3Pd^2\right)\xi_P - \xi_{tt} + 2\eta^2_{Pt} - \frac{2\eta^2_t}{P} = 0 \end{aligned} \tag{4.23f}$$

$$\begin{aligned} \frac{P^2d^3\xi_{PP}}{c} + \frac{Pbd\xi_t}{c} + \frac{Pd^2\eta^2_{PP}}{c} - \frac{2Pd^2\xi_{Pt}}{c} + \left(\frac{b}{c} + \frac{2d}{Pc}\right)\eta^2_t + \\ + \left(\frac{bd}{c} + \frac{d^2}{Pc}\right)\eta^2 + \left(-\frac{Pbd}{c} - \frac{d^2}{c}\right)\eta^2_P + \left(-\frac{P^2bd^2}{c} + \frac{Pd^3}{c}\right)\xi_P + \\ + \frac{d\xi_{tt}}{c} - \frac{2d\eta^2_{Pt}}{c} + \frac{\eta^2_{tt}}{Pc} = 0. \end{aligned} \tag{4.23g}$$

Equations (4.23a) and (4.23b) gives that

$$\xi = c_1,$$

where c_1 is an arbitrary constant. Thus the remaining eqs. (4.23c) and (4.23e) to (4.23g) simplify to

$$\frac{d\eta^2_P}{c} - \frac{d\eta^2}{Pc} - \frac{\eta^2_t}{Pc} = 0 \tag{4.24a}$$

$$Pc\eta^2_{PP} - c\eta^2_P + \frac{c\eta^2}{P} = 0 \tag{4.24b}$$

$$-2Pd\eta^2_{PP} + 2d\eta^2_P + \left(b - \frac{2d}{P}\right)\eta^2 + 2\eta^2_{Pt} - \frac{2\eta^2_t}{P} = 0 \tag{4.24c}$$

$$\begin{aligned} \frac{Pd^2\eta^2_{PP}}{c} + \left(\frac{b}{c} + \frac{2d}{Pc}\right)\eta^2_t + \left(\frac{bd}{c} + \frac{d^2}{Pc}\right)\eta^2 + \\ + \left(-\frac{Pbd}{c} - \frac{d^2}{c}\right)\eta^2_P - \frac{2d\eta^2_{Pt}}{c} + \frac{\eta^2_{tt}}{Pc} = 0. \end{aligned} \tag{4.24d}$$

Equation (4.24a) has the general solution

$$\eta^2 = F\left(Pe^{dt}\right)e^{-dt}$$

for an arbitrary univariate function F. Thus eqs. (4.24b) and (4.24c) can be further simplified to

$$Pce^{dt}F''\Big(Pe^{dt}\Big) - cF'\Big(Pe^{dt}\Big) + \frac{cF\Big(Pe^{dt}\Big)e^{-dt}}{P} = 0 \tag{4.25a}$$

$$bF\Big(Pe^{dt}\Big)e^{-dt} = 0. \tag{4.25b}$$

Thus it is clear from eq. (4.25b) that

$$F \equiv 0$$

and hence the general solution to the parameter independence determining equations (4.21) is

$$\begin{aligned} \xi &= c_1 \\ \eta^1 &= 0 \\ \eta^2 &= 0 \end{aligned}$$

which is spanned by the manifest generator

$$X_1 = \partial_t.$$

b-independent symmetries

Decomposition of eqs. (4.20) in b gives the parameter independence determining equations

$$\frac{dN}{dt}, 1: \quad -N^2a^2\xi_N + Na\eta^1_N - Na\xi_t - a\eta^1 + (NPc - Pd)\eta^1_P + \tag{4.26a}$$

$$+\Big(-N^2Pac + NPad\Big)\xi_P + \eta^1_t = 0 \tag{4.26b}$$

$$\frac{dN}{dt}, b: \quad 2N^2Pa\xi_N - NP\eta^1_N + NP\xi_t + N\eta^2 + P\eta^1 + \tag{4.26c}$$

$$+\Big(N^2P^2c - NP^2d\Big)\xi_P = 0 \tag{4.26d}$$

$$\frac{dN}{dt}, b^2: \quad -N^2P^2\xi_N = 0 \tag{4.26e}$$

$$\frac{dP}{dt}, 1: \quad Na\eta^2_N - Pc\eta^1 + (-Nc + d)\eta^2 + (-NPc + Pd)\xi_t + \tag{4.26f}$$

$$+(NPc - Pd)\eta^2_P + \Big(-N^2Pac + NPad\Big)\xi_N + \tag{4.26g}$$

$$+\Big(-N^2P^2c^2 + 2NP^2cd - P^2d^2\Big)\xi_P + \eta^2_t = 0 \tag{4.26h}$$

$$\frac{dP}{dt}, b: \quad -NP\eta^2_N + \Big(N^2P^2c - NP^2d\Big)\xi_N = 0. \tag{4.26i}$$

From eqs. (4.26e) and (4.26i) it is clear that

$$\xi = \xi(t, P) \tag{4.27a}$$

$$\eta^2 = \eta^2(t, P), \tag{4.27b}$$

and thus eq. (4.26h) can be written as

$$\eta^1 = -N^2Pc\xi_P + 2NPd\xi_P + N\eta^2_P - N\xi_t - \\ - \frac{N\eta^2}{P} - \frac{Pd^2\xi_P}{c} - \frac{d\eta^2_P}{c} + \frac{d\xi_t}{c} + \frac{d\eta^2}{Pc} + \frac{\eta^2_t}{Pc}.$$

Since neither ξ nor η^2 depends on N, and η^1 thus only depends explicitly on N, the remaining parameter independence determining equations (4.26b) and (4.26d) can be decomposed further in N resulting in the equations

$$1: \qquad \frac{P^2d^3\xi_{PP}}{c} + \frac{Pd^2\eta^2_{PP}}{c} - \frac{2Pd^2\xi_{Pt}}{c} - \frac{ad\xi_t}{c} + \tag{4.28a}$$

$$+\left(-\frac{a}{Pc} + \frac{2d}{Pc}\right)\eta^2_t + \left(\frac{ad}{c} - \frac{d^2}{c}\right)\eta^2_P + \tag{4.28b}$$

$$+\left(-\frac{ad}{Pc} + \frac{d^2}{Pc}\right)\eta^2 + \left(\frac{Pad^2}{c} + \frac{Pd^3}{c}\right)\xi_P + \tag{4.28c}$$

$$+\frac{d\xi_{tt}}{c} - \frac{2d\eta^2_{Pt}}{c} + \frac{\eta^2_{tt}}{Pc} = 0 \tag{4.28d}$$

$$N: \qquad -3P^2d^2\xi_{PP} - 2Pd\eta^2_{PP} + 4Pd\xi_{Pt} - a\xi_t + 2d\eta^2_P + \tag{4.28e}$$

$$+\left(Pad - 3Pd^2\right)\xi_P - \xi_{tt} + 2\eta^2_{Pt} - \frac{2d\eta^2}{P} - \frac{2\eta^2_t}{P} = 0 \tag{4.28f}$$

$$N^2: \qquad 3P^2cd\xi_{PP} + Pc\eta^2_{PP} - 2Pc\xi_{Pt} - c\eta^2_P + \tag{4.28g}$$

$$+(-2Pac + 3Pcd)\xi_P + \frac{c\eta^2}{P} = 0 \tag{4.28h}$$

$$N^3: \qquad -P^2c^2\xi_{PP} - Pc^2\xi_P = 0 \tag{4.28i}$$

$$b: \qquad -\frac{P^2d^2\xi_P}{c} - \frac{Pd\eta^2_P}{c} + \frac{Pd\xi_t}{c} + \frac{d\eta^2}{c} + \frac{\eta^2_t}{c} = 0 \tag{4.28j}$$

$$Nb: \qquad -P^2d\xi_P + P\xi_t + \eta^2 = 0 \tag{4.28k}$$

$$N^2b: \qquad 2P^2c\xi_P = 0. \tag{4.28l}$$

Given eq. (4.28l),

$$\xi_P = 0,$$

and thus eq. (4.28k) gives that

$$\eta^2 = -P\xi_t$$

Since the only functional dependence left is in t for the unknown function

$$\xi = \xi(t),$$

eqs. (4.28d), (4.28f) and (4.28j) can be further decomposed in P, resulting in the equations

$$1: \qquad -\frac{ad\xi'}{c} + \left(\frac{a}{c} + \frac{d}{c}\right)\xi'' - \frac{\xi'''}{c} = 0 \tag{4.29}$$

$$N: \qquad -a\xi' - \xi'' = 0 \tag{4.30}$$

$$Pb: \qquad \frac{d\xi'}{c} - \frac{\xi''}{c} = 0. \tag{4.31}$$

Unless $a = -d$, which will not be the case as both parameters are strictly positive,

$$\xi' = 0,$$

and thus

$$\xi = c_1$$

for an arbitrary constant c_1. Thus, the general solution to the parameter independence determining equations (4.26) is

$$\begin{aligned} \xi &= c_1 \\ \eta^1 &= 0 \\ \eta^2 &= 0 \end{aligned}$$

which is spanned by the manifest generator

$$X_1 = \partial_t.$$

c and d-independent symmetries

The only assumption about the parameters used in the calculations of a and b-independent symmetries are that the parameters are non-zero and that all parameters have the same sign (namely they are all positive). Using the variable and parameter substitutions

$$\begin{aligned} \tilde{N} &= P \\ \tilde{P} &= N \\ \tilde{a} &= -d \\ \tilde{b} &= -c \\ \tilde{c} &= -b \\ \tilde{d} &= -a, \end{aligned}$$

the same calculations will thus hold for finding $\tilde{a}$ and $\tilde{b}$-independent symmetries of the model after substitution, as all parameters still are non-zero and have the same sign. Substituting back to the original model, the manifest symmetry generator

$$X_1 = \partial_t$$

must thus be the only c and d-independent symmetry generator.

$\frac{dM}{dt}$,	1:	179 terms
$\frac{dM}{dt}$,	α_M:	79 terms
$\frac{dM}{dt}$,	$(\alpha_M)^2$:	3 terms
$\frac{dB}{dt}$,	1:	112 terms
$\frac{dB}{dt}$,	α_M:	6 terms
$\frac{dL}{dt}$,	1:	529 terms
$\frac{dL}{dt}$,	α_M:	42 terms
$\frac{dA}{dt}$,	1:	307 terms
$\frac{dA}{dt}$,	α_M:	18 terms
$\frac{dP}{dt}$,	1:	112 terms
$\frac{dP}{dt}$,	α_M:	6 terms

Table 4.1: Terms of the the parameter independence determining equations for α_M-independent generators.

4.4 The Yildirim–Mackey lactose operon model

As seen in the previous sections of this chapter, the naïve approach to solving the parameter independence determining equations requires guidance by a human; in general systems of first order PDE:s are not solvable in any algorithmic manner. Additionally, as was seen in chapter 3 the linearized symmetry condition grows quickly with additional states. As a consequence, it becomes unviable to solve the parameter independence determining equations for the Yildirim–Mackey lactose operon model the naïve way. Not only will the decomposed equations be hard to get an overview on, leading to time consuming selection processes for the "next step" in the calculations. The amount of calculations required will also grow as the amount of parameters of a model generally grows together with the number of states.

To exemplify this, the number of terms in the parameter independence determining equations for α_M-independent generators is shown in table 4.1. In the process of refining forms of the unknown functions $\xi, \eta^1, \ldots, \eta^5$, each of these terms might in the worst case decompose into individual equations to be solved. This extreme case would of course be easy to solve as all available undetermined functions and derivatives would have to be zero everywhere, but it nonetheless gives an upper bound on the number of the equations in the systems resulting from using the naïve approach. For certain forms of equations, some first steps of simplification can be done algorithmically. Looking at the earlier calculations for the Gompertz and Lotka–Volterra models, most have a common first step of eliminating dependence in one of the states for ξ and all but one of the η^i functions (see eqs. (4.17) and (4.18) and eqs. (4.22) and (4.27)). This pattern, which also fits for α_M-independence, holds when only one equation (eq. (1.18a)) of the system of equations (eqs. (1.18)) is dependent on a parameter (α_M) linearly. If those conditions are true, ξ and all but one of the equations η^i will not be dependent on a state. In the case of α_M-independence, only η^1 can be dependent on M. While this knowledge simplifies the

$$\begin{array}{rr}
\frac{dM}{dt},\ 1: & 170 \text{ terms}\\
\frac{dM}{dt},\ \alpha_M: & 71 \text{ terms}\\
\frac{dB}{dt},\ 1: & 100 \text{ terms}\\
\frac{dL}{dt},\ 1: & 445 \text{ terms}\\
\frac{dA}{dt},\ 1: & 271 \text{ terms}\\
\frac{dP}{dt},\ 1: & 100 \text{ terms}
\end{array}$$

Table 4.2: Terms of the the parameter independence determining equations for α_M-independent generators after an easy to find simplification.

parameter independence determining equations the determining system is still large, as seen in table 4.2, and not viable to solve the naïve way.

Chapter 5

The interpretation and structure of symmetries in biology

In the previous two chapters, two different methods were used to find symmetries of parametrized first order ODE:s. However, finding symmetries has little to no value unless they can be used to better understand biological processes. While some of the possible uses for symmetries have been mentioned in passing in earlier chapters, this chapter intends to explore these ideas more fully. The chapter consists of two parts. In the first introductory part, an overview of how symmetries could fit into biological modeling is presented. Most ideas are open ended, as they constitute one or several research projects on their own. In the second part, one such use, namely the interpretation of symmetries as relating to invariants of the differential system, is explored for the biological models for which symmetries have been found. It turns out, based on the mathematics in section 2.4, that the relation between invariants of the differential system and the symmetries thereof is quite straight forward for first order ODE systems.

5.1 Symmetries as a tool in modeling

Three of the larger obstacles when constructing biological models are model construction, model validation and model selection. There is potential for symmetries to be used to address all these three areas of modeling.

Model construction is the process of going from biological knowledge to a mathematical model. In this process, models are often built from first principles and are simplified by making additional assumptions, also known as model reduction. If a proper theory of symmetries in biology were to exist, symmetries could potentially be used to enhance this process. The selection of appropriate first principles could be enhanced by knowing invariant and symmetric properties of those first principles. Additionally, model reduction could be better understood during model construction by looking at which symmetries are preserved during reduction and which are broken. These and similar methods could essentially act as a form of pre-screening for the model validation.

Model validation is the process of comparing the mathematical model developed in model construction to experimental data. In the case of ODE models such as those studied in this thesis, the available data will be several time series of measurements of the system studied. Even for non-parametrized ODE models, the process of obtaining predictive estimates from the model is not trivial as non-linear systems of ODE:s do not generally have analytic solutions. Instead, a numerical estimation must be performed, which depending on the ODE system might be computationally costly. To further complicate matters, such simulations are not possible to perform for general parametrized models, as concrete parameter values are needed. Instead, the parameters must be considered statistically at the same time as the model is simulated. This process is substantially more computationally costly, and must be reperformed every time the model is changed. As symmetries can be used to partially or completely solve differential equations, it would be of interest to study if this could be used to reduce the computations involved in this process. Symmetries could also be used as another form of pre-screening, comparing symmetries of the model to symmetries of the data. This hinges on the calculations of symmetries being significantly less computationally costly than those of parameter estimation.

If that is not the case, symmetries could still be used during model selection, where several models that all fit available data must be selected amongst. More costly symmetry calculations could in this step be used to compare model fit to data transformed with symmetries, thus differentiating between models where traditional methods fail [9]. Common to all of the applications of symmetries after the fact that data is introduced is the question of how parameters should be treated. As previously mentioned there is an uncertainty around the parameters that is taken into account when evaluating models. Symmetries as treated in this thesis ignore all probabilistic properties of both the models themselves and of parameters. To properly apply symmetries in these contexts, more general theory has to be used to take such properties into account.

This also raises the question of whether parameters in symmetry generators are desirable or not. When using and seeing symmetries as relating to fundamental biological concepts, symmetry generators containing few or no parameters could be considered more useful, as fewer parameters of the model has to be fixed for a generator to relate to concrete transformations. Such symmetries would then correspond to more general biological concepts. An example of this is the symmetry generated by ∂_t, corresponding to time invariance. As the symmetry is not dependent on any parameter, a common interpretation can be made for all models: the symmetry signals that the system evolves independently of factors dependent on time. For every parameter in a generator, more assumptions on the model in question are needed; a meaningful interpretation of the symmetry can not be made until an interpretation of the parameters exist.

On the other hand, parameters in symmetry generators is what would make differentiation between similar models in model selection possible. A productive way to think about these concepts is to view parametrized models as sets of models. The question of whether parameters in symmetry generators are desirable or not then simplifies to the question of whether the use of the symmetry is to differentiate between subsets of this set of models, or to describe properties of the entire set of models.

5.2 Invariant solutions under symmetry of the Hill equation

To better understand the underlying source of the Lie symmetry groups of the Hill equation, it is of interest to find curves invariant under the solution. The reduced characteristic of the generator

$$X_2 = -((n-1)x + ny)\partial_\tau + y\partial_y$$

is

$$\begin{aligned}\bar{Q} = \eta - \omega\xi = y - \left(-\frac{y^n}{1+y^2}\right)(-((n-1)\tau + ny)) = \\ = y\left(1 - \frac{y^{n-1}((n-1)\tau + ny)}{1+y^2}\right).\end{aligned}$$

Since solutions are invariant under a symmetry if the characteristic is 0 on the entire solution curve, invariant solutions must satisfy

$$y\left(1 - \frac{y^{n-1}((n-1)\tau + ny)}{1+y^n}\right) = 0.$$

The solutions that meet this condition (aside from the trivial case $y \equiv 0$) must thus be on the form

$$y^{n-1}((n-1)\tau + ny) = 1 + y^n,$$

which is more clearly stated as

$$(n-1)\left(\tau y^{n-1} + y^n\right) = 1.$$

For all $n > 0$ except $n = 1$ such solutions exist, and take the form

$$\tau y^{n-1} + y^n = \frac{1}{n-1}. \tag{5.1}$$

Additionally, since τ is (dimensionless) time, any application of the model will have an initial condition on the form $y(0) = y_0$. By fixing $\tau = 0$ in eq. (5.1), the initial condition of an invariant curve given any $n > 0, n \neq 1$ is shown to be

$$y(0) = \frac{1}{(n-1)^{1/n}}.$$

5.3 The structure of the symmetry groups of the Gompertz models

As discussed in section 2.4, all symmetries of first order systems of ODE:s can be separated in to two parts: the trivial component and the characteristic component. Furthermore, the characteristic component's general form depends only on the invariants of the differential system. Here this connection will be shown explicitly for all formulations of the Gompertz model, serving both as a case study and as a further investigation of the different formulations of the Gompertz model.

5.3.1 The classical Gompertz model

The symmetries of the classical Gompertz model found using an ansatz in chapter 3 were

$$\begin{aligned}
X_{\mathrm{c},1} &= e^{k_G t}\partial_t \\
X_{\mathrm{c},2} &= W e^{k_G t + e^{T_i k_G} e^{-k_G t}}\partial_t \\
X_{\mathrm{c},3} &= e^{-e^{T_i k_G} e^{-k_G t}}\partial_W \\
X_{\mathrm{c},f} &= \frac{f(t) e^{-T_i k_G} e^{k_G t}}{k_G}\partial_t + W f(t)\partial_W
\end{aligned}$$

and the symmetries found using parameter independence in chapter 4 were

$$\begin{aligned}
X_{\mathrm{c},1} &= e^{k_G t}\partial_t \\
X_{\mathrm{c},4} &= W\partial_W \\
X_{\mathrm{c},5} &= \partial_t - k_G W \ln(W)\partial_W .
\end{aligned}$$

The corresponding reduced characteristics of the symmetry generators are

$$\begin{aligned}
\bar{Q}_{\mathrm{c},1} &= -k_G e^{k_G T_i} W \\
\bar{Q}_{\mathrm{c},2} &= -k_G e^{k_G T_i + e^{-k_G (t-T_i)}} W^2 \\
\bar{Q}_{\mathrm{c},3} &= e^{-e^{-k_G (t-T_i)}} \\
\bar{Q}_{\mathrm{c},4} &= W \\
\bar{Q}_{\mathrm{c},5} &= -k_G W \ln(W) - k_G e^{-k_G (t-T_i)} W \\
\bar{Q}_{\mathrm{c},f} &= 0.
\end{aligned}$$

Thus it is clear that the symmetry generator $X_{\mathrm{c},f}$ is a trivial symmetry generator. From the mathematical theory the reduced characteristic of any symmetry generator can be written as

$$\bar{Q} = (\partial_W J)^{-1} I,$$

where J consists of functionally independent invariants and I is any invariant. As the classical Gompertz model is a scalar first order ODE, the J is one-dimensional, and thus the quotient of two reduced characteristics must be an invariant. Picking the reduced characteristics $\bar{Q}_{\mathrm{c},4}$ and $\bar{Q}_{\mathrm{c},5}$ that differ by more than a constant expression (assuming the parameters are constant),

$$\frac{\bar{Q}_{\mathrm{c},5}}{\bar{Q}_{\mathrm{c},4}} = -k_G\Big(\ln(W) + e^{-k_G (t-T_i)}\Big) = I$$

is an invariant since

$$X_{\mathrm{c},\mathrm{T}}(I) = I_t + k_G e^{-k_G (t-T_i)} W I_W = k_G^2 e^{-k_G (t-T_i)} - k_G e^{-k_G (t-T_i)} W \frac{k_G}{W} = 0.$$

For the particular case of scalar first order equations with known solutions such as the classical Gompertz ODE, the above described methodology is not the most direct path to finding such an invariant. The formulation

$$I_t + k_G e^{-k_G(t-T_i)} W I_W = 0$$

of the invariance condition can be solved using the method of characteristics, which reformulates the problem as

$$\frac{dt}{1} = \frac{dW}{k_G e^{-k_G(t-T_i)} W}$$

which simplifies to

$$d\Big(e^{-k_G(t-T_i)} + \ln(W)\Big) = 0$$

leading to the equivalent invariant. Returning to the task of determining the general structure of the group of all symmetries,

$$J(t,W) = e^{-k_G(t-T_i)} + \ln(W)$$

can be taken. Thus

$$\partial_W J = \frac{1}{W}$$

and

$$(\partial_W J)^{-1} = W.$$

Similarly, an arbitrary invariant I of the differential equation can be written as

$$I(t,W) = F\Big(e^{-k_G(t-T_i)} + \ln(W)\Big)$$

for and arbitrary function F. Thus, the reduced characteristic of any symmetry generator must have the form

$$\bar{Q} = WF\Big(e^{-k_G(t-T_i)} + \ln(W)\Big) \tag{5.2}$$

and the general form for a symmetry generator is

$$X = \xi(t,W)\partial_t + W\Big(k_G e^{-k_G(t-T_i)}\xi(t,W) + F\Big(e^{-k_G(t-T_i)} + \ln(W)\Big)\Big)\partial_W \tag{5.3}$$

for arbitrary functions ξ and F.

5.3.2 The autonomous Gompertz model

The symmetries of the autonomous Gompertz model found using an ansatz in chapter 3 were

$$\begin{aligned}
X_{\mathrm{a},1} &= e^{k_G t} \ln\Big(\frac{W}{A}\Big)\partial_t \\
X_{\mathrm{a},2} &= e^{-k_G t} W \partial_W \\
X_{\mathrm{a},3} &= \ln\Big(\frac{W}{A}\Big) W \partial_W \\
X_{\mathrm{a},f} &= f(t)\partial_t - k_G f(t) \ln\Big(\frac{W}{A}\Big) W \partial_W
\end{aligned}$$

and the symmetries found using parameter independence in chapter 4 were

$$\begin{aligned}
X_{\mathrm{a},2} &= e^{-k_G t} W \partial_W \\
X_{\mathrm{a},3} &= \ln\left(\frac{W}{A}\right) W \partial_W \\
X_{\mathrm{a},4} &= \partial_t \\
X_{\mathrm{a},5} &= t\partial_t + \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) \ln\left(\frac{W}{A}\right) W \partial_W \\
X_{\mathrm{a},6} &= e^{-k_G t}\partial_t - k_G e^{-k_G t} \ln(W) W \partial_W .
\end{aligned}$$

The corresponding reduced characteristics of the symmetry generators are

$$\begin{aligned}
\bar{Q}_{\mathrm{c},1} &= k_G e^{k_G t} \left(\ln\left(\frac{W}{A}\right)\right)^2 W \\
\bar{Q}_{\mathrm{c},2} &= e^{-k_G t} W \\
\bar{Q}_{\mathrm{c},3} &= \ln\left(\frac{W}{A}\right) W \\
\bar{Q}_{\mathrm{c},4} &= k_G \ln\left(\frac{W}{A}\right) W \\
\bar{Q}_{\mathrm{c},5} &= \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) \ln\left(\frac{W}{A}\right) W + k_G t \ln\left(\frac{W}{A}\right) W \\
\bar{Q}_{\mathrm{c},6} &= -k_G \ln(A) e^{-k_G t} W \\
\bar{Q}_{\mathrm{c},f} &= 0.
\end{aligned}$$

Just as for the classical Gompertz model, there are several ways to find a function J consisting of functionally independent invariants of the autonomous Gompertz model. Using the most straight-forward method,

$$\frac{\bar{Q}_{\mathrm{c},5}}{\bar{Q}_{\mathrm{c},3}} = \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) + k_G t$$

is an invariant, and thus

$$J(t, W) = \ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) + k_G t$$

can be chosen. Thus

$$\partial_W J = \frac{1}{\ln\left(\frac{W}{A}\right) W}$$

and

$$(\partial_W J)^{-1} = \ln\left(\frac{W}{A}\right) W.$$

Using corollary 2.4.2, the reduced characteristic of symmetry generators of the autonomous Gompertz model thus has the general form

$$\bar{Q} = \ln\left(\frac{W}{A}\right) W F\left(\ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) + k_G t\right), \tag{5.4}$$

where F is an arbitrary function, with the general form for a symmetry generator being

$$X = \xi(t,W)\partial_t + \ln\left(\frac{W}{A}\right)W\left(-k_G\xi(t,W) + F\left(\ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) + k_G t\right)\right)\partial_W \tag{5.5}$$

for arbitrary functions ξ and F.

5.3.3 The system Gompertz model

The symmetries of the system Gompertz model found using an ansatz in chapter 3 were

$$\begin{aligned}
X_{\text{s},1} &= \partial_t \\
X_{\text{s},2} &= -\frac{e^{k_G t}}{k_G}\partial_t + Ge^{k_G t}\partial_G \\
X_{\text{s},3} &= e^{k_G t}G\partial_t \\
X_{\text{s},4} &= W\partial_W \\
X_{\text{s},5} &= -\frac{We^{-k_G t}}{k_G}\partial_W + e^{-k_G t}\partial_G
\end{aligned}$$

and the symmetries found using parameter independence in chapter 4 were

$$\begin{aligned}
X_{\text{s},1} &= \partial_t \\
X_{\text{s},4} &= W\partial_W \\
X_{\text{s},6} &= \ln(W)W\partial_W + G\partial_G.
\end{aligned}$$

The corresponding reduced characteristics of the symmetry generators are

$$\begin{aligned}
\bar{\boldsymbol{Q}}_{\text{s},1} &= (-WG, k_G G) \\
\bar{\boldsymbol{Q}}_{\text{s},2} &= \left(\frac{e^{k_G t}}{k_G}WG, 0\right) \\
\bar{\boldsymbol{Q}}_{\text{s},3} &= \left(-e^{k_G t}WG^2, k_G e^{k_G t}G^2\right) \\
\bar{\boldsymbol{Q}}_{\text{s},4} &= (W, 0) \\
\bar{\boldsymbol{Q}}_{\text{s},5} &= \left(-\frac{We^{-k_G t}}{k_G}, e^{-k_G t}\right) \\
\bar{\boldsymbol{Q}}_{\text{s},6} &= (\ln(W)W, G).
\end{aligned}$$

Since the system Gompertz model has two equations, two functionally independent invariants exist. While it is a bit more cumbersome than in the scalar case to calculate invariants from the reduced characteristics, it is still possible. However, in the particular case of the system Gompertz ODE, using the method of characteristics to solve the invariance condition is also a viable approach. Both methods will be shown here to exemplify how the calculations are made for non-scalar ODE:s.

Using the reduced characteristics, one invariant can be found using the fact that

$$\bar{\boldsymbol{Q}}_{\mathrm{s},3} = e^{k_G t} G(-WG, k_G G) = e^{k_G t} G \bar{\boldsymbol{Q}}_{\mathrm{s},1}$$

implies that $e^{k_G t} G$ is an invariant. Using this invariant, all of the reduced characteristics $\bar{\boldsymbol{Q}}_{\mathrm{s},1}, \dots, \bar{\boldsymbol{Q}}_{\mathrm{s},5}$ found using the ansatz method can be divided into two sets of vectors that only differ by invariant coefficients.

$$\begin{aligned} \bar{\boldsymbol{Q}}_{\mathrm{s},1} &= \frac{\bar{\boldsymbol{Q}}_{\mathrm{s},3}}{e^{k_G t} G} = \left(k_G e^{k_G t} G\right) \bar{\boldsymbol{Q}}_{\mathrm{s},5} \\ \frac{e^{k_G t} G}{k_G} \bar{\boldsymbol{Q}}_{\mathrm{s},2} &= \bar{\boldsymbol{Q}}_{\mathrm{s},4}. \end{aligned}$$

Since no function f could result in the relationship $-\bar{\boldsymbol{Q}}_{\mathrm{s},1} = f(t, W, G) \bar{\boldsymbol{Q}}_{\mathrm{s},4}$,

$$\begin{pmatrix} W & WG \\ 0 & -k_G G \end{pmatrix} = \left(\partial_{(W,G)} \boldsymbol{J}\right)^{-1}$$

must hold for some function J consisting of functionally independent invariants. Thus a valid J is the solution to the differential equation

$$\partial_{(W,G)} \boldsymbol{J} = \begin{pmatrix} W & WG \\ 0 & -k_G G \end{pmatrix}^{-1} \tag{5.6}$$

that also fulfills the original invariance condition

$$\partial_{(t,W,G)} \boldsymbol{J} \cdot \begin{pmatrix} 1 \\ WG \\ -k_G G \end{pmatrix} = 0.$$

Thus, finding a J consisting of functionally independent invariants using only the reduced characteristics $\bar{\boldsymbol{Q}}_{\mathrm{s},1}, \dots, \bar{\boldsymbol{Q}}_{\mathrm{s},5}$ found using the ansatz method is essentially the problem of finding invariants, but with eq. (5.6) serving as a hint. But, using the reduced characteristic $\bar{\boldsymbol{Q}}_{\mathrm{s},6}$ found using the parameter independence method, this calculation can be avoided since

$$\begin{aligned} \bar{\boldsymbol{Q}}_{\mathrm{s},6} = (\ln(W)W, G) = \left(-\frac{WG}{k_G}, G\right) + \left(\ln(W)W + \frac{WG}{k_G}, 0\right) &= \\ = \frac{1}{k_G} \bar{\boldsymbol{Q}}_{\mathrm{s},1} + \left(\ln(W) + \frac{G}{k_G}\right) \bar{\boldsymbol{Q}}_{\mathrm{s},4}&. \end{aligned}$$

$\ln(W) + \frac{G}{k_G}$ must thus be an invariant, and since $e^{k_G t} G$ and $\ln(W) + \frac{G}{k_G}$ are functionally independent,

$$\boldsymbol{J}(t, W, G) = \left(\ln(W) + \frac{G}{k_G}, \ln\left(e^{k_G t} G\right)\right) = \left(\ln(W) + \frac{G}{k_G}, k_G t + \ln(G)\right)$$

must consist of functionally independent invariants.

Using the method of characteristics to solve the invariance condition

$$I_t + WGI_W - k_G G I_G = 0,$$

results in the reformulated problem

$$\frac{dt}{1} = \frac{dW}{WG} = \frac{dG}{-k_G G}.$$

The expression

$$\frac{dW}{WG} = \frac{dG}{-k_G G}$$

simplifies to

$$d\left(\ln(W) + \frac{G}{k_G}\right) = 0,$$

while

$$\frac{dt}{1} = \frac{dG}{-k_G G}$$

simplifies to

$$d(k_G t + \ln(G)) = 0.$$

Thus

$$\boldsymbol{J}(t, W, G) = \left(\ln(W) + \frac{G}{k_G}, k_G t + \ln(G)\right), \tag{5.7}$$

consisting of functionally independent invariants, is once again found.

Using the J in (5.7),

$$\partial_{(W,G)}\boldsymbol{J} = \begin{pmatrix} \frac{1}{W} & \frac{1}{k_G} \\ 0 & \frac{1}{G} \end{pmatrix}$$

and thus

$$\left(\partial_{(W,G)}\boldsymbol{J}\right)^{-1} = \begin{pmatrix} W & -\frac{WG}{k_G} \\ 0 & G \end{pmatrix}.$$

Using corollary 2.4.2, the reduced characteristic of any symmetry generator must thus have the form

$$\bar{\boldsymbol{Q}} = \begin{pmatrix} W & -\frac{WG}{k_G} \\ 0 & G \end{pmatrix} \cdot \begin{pmatrix} F_1\left(\ln(W) + \frac{G}{k_G}, k_G t + \ln(G)\right) \\ F_2\left(\ln(W) + \frac{G}{k_G}, k_G t + \ln(G)\right) \end{pmatrix}, \tag{5.8}$$

where F_1 and F_2 are arbitrary functions. The general form of Lie point symmetry generators of the system Gompertz model is thus

$$\begin{aligned} X =& \xi(t, W, G)\partial_t + \\ &+ \left(WG\xi(t, W, G) + WI_1(t, W, G) - \frac{WG}{k_G} I_2(t, W, G)\right)\partial_W + \\ &+ (-k_G G\xi(t, W, G) + GI_2(t, W, G))\partial_G, \end{aligned}$$

where ξ is an arbitrary function and

$$\begin{aligned} I_1(t,W,G) &= F_1\Big(\ln(W)+\frac{G}{k_G}, k_G t+\ln(G)\Big) \\ I_2(t,W,G) &= F_2\Big(\ln(W)+\frac{G}{k_G}, k_G t+\ln(G)\Big) \end{aligned}$$

are invariants.

5.3.4 Comparison of the Gompertz models

With the general forms of the Gompertz model Lie point symmetries established, further insight to the relationship between the three models can be gained. Since both the classical and the autonomous model exist in the same space ($B \simeq \mathbb{R}(t)$ and $F \simeq \mathbb{R}(W)$), comparison between the scalar models is a natural starting point.

The trivial symmetry generator

$$X_{\mathrm{a,T}} = \partial_t - k_G \ln\Big(\frac{W}{A}\Big) W \partial_W$$

of the autonomous Gompertz model is symmetry of the classical Gompertz model, since

$$-k_G \ln\Big(\frac{W}{A}\Big) W = W\Big(k_G e^{-k_G(t-T_i)} - k_G\Big(e^{-k_G(t-T_i)} + \ln(W)\Big) + k_G\ln(A)\Big),$$

and thus $X_{\mathrm{a,T}}$ can be written on the general form eq. (5.3) of classical Gompertz symmetries, with $F(x) = -k_G x + k_G \ln(A)$ and $\xi(t,W) \equiv 1$. Similarly, the trivial symmetry generator

$$X_{\mathrm{c,T}} = \partial_t + k_G e^{-k_G(t-T_i)} W \partial_W$$

of the classical Gompertz model can be written on the general form eq. (5.5) of autonomous Gompertz symmetries, since

$$k_G e^{-k_G(t-T_i)} W = \ln\Big(\frac{W}{A}\Big) W \Big(-k_G + k_G e^{k_G T_i} e^{-\left(\ln\left(\left|\ln\left(\frac{W}{A}\right)\right|\right) + k_G t\right)} + k_G\Big).$$

The parameter k_G is assumed to have the same value in both models for these statements to hold, which is reasonable since the parametrization of all three models is done in such a way that k_G has the same effect on solution curves. It is also worth noting that the parameters A and T_i are arbitrary values for the classical and autonomous Gompertz models respectively; they have no relation to the properties they represent when they are not part of the ODE formulation. As long as A is considered an invariant of the classical Gompertz model and T_i is considered an invariant of the autonomous Gompertz model, the arbitrary invariant multipliers of the characteristic components $X_{\mathrm{c},\bar{\boldsymbol{Q}}}$ and $X_{\mathrm{a},\bar{\boldsymbol{Q}}}$ of the respective symmetries can be chosen so that the vector field corresponding to the autonomous model is a symmetry of the classical model and vice versa.

The system Gompertz model can not as stringently be compared to the scalar models. However, by using some intuition the connection between the models and their symmetries can be shown to be quite straight forward. Consider first the classical model and the system model. In this case, G is “equal” to $k_G e^{-k_G(t-T_i)}$. The general form of the reduced characteristic for the classical model (5.2) can then be seen as the first column and first invariant in the general form of the reduced characteristic for the system model (5.8), since

$$\bar{Q}_{\mathrm{c}} = WF\Big(e^{-k_G(t-T_i)} + \ln(W)\Big)$$

then has the same form as

$$\bar{\boldsymbol{Q}}_{\mathrm{s}} = \begin{pmatrix} W \\ 0 \end{pmatrix} \cdot F_1\bigg(\ln(W) + \frac{G}{k_G}\bigg). \tag{5.9}$$

Instead considering the autonomous and the system model, G is “equal” to $-k_G \ln\Big(\frac{W}{A}\Big)W$ The general form of the reduced characteristic for the autonomous model (5.4) can then be seen as the second column and second invariant in the general form of the reduced characteristic for the system model (5.8), since

$$\bar{Q}_{\mathrm{a}} = \ln\bigg(\frac{W}{A}\bigg)WF\bigg(\ln\bigg(\bigg|\ln\bigg(\frac{W}{A}\bigg)\bigg|\bigg) + k_G t\bigg)$$

then has the same form as

$$\bar{\boldsymbol{Q}}_{\mathrm{s}} = \begin{pmatrix} -\frac{WG}{k_G} \\ G \end{pmatrix} \cdot F_2(k_G t + \ln(G)). \tag{5.10}$$

Together, eq. (5.9) and eq. (5.10) make up a subset of the general form in eq. (5.8) of the reduced characteristic for the system Gompertz model. The two functions F_1 and F_2 only depend on one invariant each in the comparison to the symmetries of the scalar models, as opposed to both invariants in the general form for the system Gompertz model. As such, the symmetries of the system model capture more than the sum of the symmetries of the two scalar models.

5.4 The structure of the symmetry group of the Lotka–Volterra model

The symmetries of the Lotka–Volterra model found using an ansatz in chapter 3 were

$$\begin{aligned}
X_1 &= \partial_t \\
X_2 &= \frac{-bNP + aN}{c}\partial_N + \frac{cNP - dP}{c}\partial_P \\
X_3 &= \frac{t}{c}\partial_t + \frac{-btNP + atN}{c}\partial_N + \frac{ctNP - dtP}{c}\partial_P \\
X_4 &= \frac{N}{c}\partial_t + \frac{-bcN^2P + acN^2 - bdNP + adN}{c^2}\partial_N + \frac{c^2N^2P - d^2P}{c^2}\partial_P \\
X_5 &= \frac{P}{c}\partial_t + \frac{-bNP^2 + aNP}{c}\partial_N + \frac{cNP^2 - dP^2}{c}\partial_P
\end{aligned}$$

and the symmetries found using parameter independence in chapter 4 were

$$X_1 = \partial_t.$$

The corresponding reduced characteristics of the symmetry generators are

$$\begin{aligned}
\bar{\boldsymbol{Q}}_1 &= -(aN - bNP, cNP - dP)\\
\bar{\boldsymbol{Q}}_2 &= \frac{1}{c}(aN - bNP, cNP - dP)\\
\bar{\boldsymbol{Q}}_3 &= 0\\
\bar{\boldsymbol{Q}}_4 &= \frac{d}{c^2}(aN - bNP, cNP - dP)\\
\bar{\boldsymbol{Q}}_5 &= 0.
\end{aligned}$$

Thus only one of the potentially two forms of reduced characteristic (modulo multiplication by invariants) is found. Furthermore, the reduced characteristics reveal no invariants by themselves.

Using the method of characteristics, one such invariant can be found with ease. The invariance condition

$$I_t + (aN - bNP)I_N + (cNP - dP)I_P = 0$$

results in the reformulated problem

$$\frac{dt}{1} = \frac{dN}{aN - bNP} = \frac{dP}{cNP - dP}. \tag{5.11}$$

The second equality can be simplified to

$$\frac{dN}{N}(cN - d) = \frac{dP}{P}(a - bP)$$

which has the solution

$$d(cN + bP - d\ln(N) - a\ln(P)) = 0. \tag{5.12}$$

The first equality in eq. (5.11) does not have an explicit solution, for the same reason the Lotka–Volterra system itself does not have an explicit solution, but must instead be studied mostly using the invariant in eq. (5.12) [33].

Using the characteristics and invariants easily calculable, it can thus be concluded that all reduced characteristics

$$\bar{\boldsymbol{Q}} = F(cN + bP - d\ln(N) - a\ln(P))(aN - bNP, cNP - dP)$$

correspond to symmetry generators of the Lotka–Volterra predator prey model (1.17), where F is an arbitrary function. All generators on the form

$$\begin{aligned}
X =&\xi(t, N, P)\partial_t +\\
&+ (aN - bNP)(\xi(t, N, P) + F(cN + bP - d\ln(N) - a\ln(P)))\partial_W +\\
&+ (cNP - dP)(\xi(t, N, P) + F(cN + bP - d\ln(N) - a\ln(P)))\partial_W
\end{aligned}$$

are thus symmetry generators of the Lotka–Volterra model.

Chapter 6

Discussion

In this chapter, in depth discussion about specific parts of the thesis will follow. Readers that are only interested in the overarching conclusions about the use of symmetries for modeling in biology are referred to the last section, section 6.4.

6.1 The parameter independence method

In chapter 4 the method of parameter independence was introduced as an alternative to ansatz testing for solving the linearized symmetry condition for first order ODE:s. The method tackles two related problems of ansatz testing: the lack of a stopping point and the lack of value from "failed" calculations. Similarly to ansatz testing, the method solves the fundamental problem of the linearized symmetry condition having an infinite amount of and often hard to find solutions by looking for specific subsets of solutions. But instead of limiting the forms of solutions by their dependency on time and states, as is the case with ansatz testing, the forms of the solutions are limited by their dependency of parameters. Interpretations of a family of symmetries corresponding to generators independent of a particular state, which is an ansatz that could be made, lead to very general statements about which states have what types of interactions. Conversely, interpretations of symmetries corresponding to generators independent of a parameter are very specific, given that the parameter has biological meaning; such symmetries are symmetries of the entire family of systems where the parameter is not fixed.

As seen in chapter 5, the parameter independence method can lead to symmetries not found using ansätze that have value in later calculations. To properly analyze the value of the parameter independence method in its current form, a larger class of models would have to be studied, and a more complete heuristic approach to ansatz testing would have to be used. More information about the use cases for the symmetries would also affect such an analysis: should two symmetries that relate to the same underlying invariant, as seen for the Lotka–Volterra model in chapter 5, be seen as the same symmetry or separate for the purposes of such a study? However, even if the method was not to produce significant new symmetries compared to heuristic ansatz testing in most cases, the theory around the method could have theoretical value, as it is a specialized application of the more general theory of the group classification introduced by Ovsiannikov [31]. Utilization of the more general theory in the context of the parameter independence method could have significant value, as it could be used to study more general model families, where parameters can be functions of states. Additionally, a common differentiation in modeling of populations is that between population parameters and parameters of a single individual. Extensions of the theory could potentially be used to improve the study of variability between individuals.

Since the method has a clear stopping condition (calculating all symmetries independent of at least one parameter), the method also produces meaningful negative results. For the Lotka–Volterra predator prey model, the only Lie point symmetry group independent of any parameters (modulo trivial symmetries) is time invariance, generated by ∂_t. It was also the only symmetry group found using the ansatz, but the difference in the conclusions that can be drawn are stark. Using an ansatz, the only conclusion from the calculations is that apart from the manifest symmetry generated by ∂_t, no fundamentally different group of Lie symmetries can be obtained from generators on the form eqs. (3.18) of the ansatz. Using the parameter independence method on the other hand, the conclusion is that using the parametrization in eqs. (1.17) of the Lotka-Volterra model, the family of systems it represents can not be subdivided by any parameter into subfamilies that have additional symmetric properties. Thus, the lack of symmetries gives a deeper understanding of the symmetric properties of the model.

Still, the method has some limitations. While the minimum number of parameter independence determining equations is $2s + 1$ where s is the number of states, compared to the s equations of the linearized symmetry condition, the resulting system is still a system of partial differential equations. Additionally, even for first order ODE:s, the number of partial derivatives in the parameter independence determining equations scales by $(s + 1)^2$ ($s + 1$ unknown functions and $s + 1$ states and time to derive in). While linear algebra can be used to classify systems of algebraic equations as over- and underdetermined, the differential properties of differential equations mean that such distinctions can not be made for the determining equations. Without delving deeper into the corresponding theory for differential equations, it is still clear that the potential for the partial derivatives to scale in number faster than the equations poses a problem. Whether these theoretical bounds pose a practical problem for typical models is essential to understand before the parameter independence method can be automated.

6.2 Solving determining equations and computer assistance

Using both ansätze and the parameter independence method in chapter 3 and chapter 4 respectively, the calculations required quickly get unviable to solve purely by hand when the models and ansätze grow. In this thesis this problem was solved by using computer algebra to keep track of calculations. The calculations were however not fully automated, due to several factors. First and foremost, such automation is outside the scope of this thesis and would take some time to implement properly. But additionally, such an implementation would not be trivial. As mentioned in the previous section, the determining equations resulting from the parameter independence method are PDE:s, and as such can not generally be solved analytically. Similarly, more general ansätze such as the one used for the Hill equation in section 3.1 also result in ansatz determining equations on the form of differential equations. An automated system should therefore be able to handle at least the common cases of differential forms if the equations are solvable. Both to determine solvability and to solve the equations, related theory such as the theory of involution need be used [34]. Since the determining equations have a highly regular form compared to general differential equations, it is not at all impossible to imagine at least specific types of determining equations being solvable using such methods.

A deeper theoretical understanding of the computational aspect of symmetries is also important for scaling the calculations. In this thesis SymPy [35] was used to perform the computer algebra; being implemented in Python, the speed of the calculations is not optimal. Additionally, many parts of the calculations are performed using general purpose functions, which means that a more specialized implementation could probably lead to speed-ups. Even weighing in these factors, it is clear that the naïve algorithms used in this thesis scale poorly with growing system size. In section 3.4 the ansatz used had to be limited to a linear one, purely due to computational limitations. As there are many models of greater size than the Yildirim–Mackey lactose operon model, even with performance improvements from using more specialized programming languages and functions, the fundamental algorithms need to be changed for the calculations to scale properly.

6.3 The structure of first order ODE symmetry groups

The calculations of the structure of the symmetry generators for some of the models in chapter 5 generate some interesting results that are worth discussing further.

For the Gompertz models, the most general structure of the symmetry generators were calculated. The two scalar models, the classical and autonomous Gompertz models, each have one non-trivial symmetric property in accordance with the theory established in section 2.4. Each such symmetric property relates to an infinite amount of symmetry generators for each of the models, obtained by multiplying a base generator with an arbitrary function of an invariant of the system. The two scalar models' symmetric properties correspond directly to the two symmetric properties of the system Gompertz model. Thus, the two scalar formulations of the model are specializations of the system formulation, differing in which symmetric property is preserved. This is in clear parallel to viewing the two scalar models as the system Gompertz model, but with one of the two boundary conditions of the problem fixed. The boundary conditions will, for the system Gompertz model, determine the values of A and T_i in the solution curve

$$W(t) = Ae^{-e^{-k_G(t-T_i)}}$$

or A and W_0 in

$$W(t) = A\left(\frac{W_0}{A}\right)^{-e^{-k_G t}}$$

depending on the parametrization. Fixing the time of inflection T_i or the size relative to the upper asymptote $\frac{W_0}{A}$ at time $t = 0$ clearly eliminates time invariance, and thus the classical Gompertz model loses the time invariance generated by ∂_t of the system Gompertz model, independent of the parametrization. Similarly, the generator $W\partial_W$ should be associated to fixing the upper asymptote A. By viewing $W\partial_W$ as the property that growth is proportional to size this association becomes clear; fixing the upper asymptote A, the scale of the growth is fixed.

Whether the classical, autonomous or system Gompertz model is most suitable for modeling a particular system comes down to whether which, or both, of these properties are desired. As a model for limb growth for an animal, time invariance is not a necessary property; the limb could not as well start growing in a month, and the progression towards maturity of an animal is often a known factor. For such situations the classical Gompertz model describes the system more correctly. The remaining symmetry of growth relating to size then corresponds to the same growth pattern being observed for specimen of different size. Conversely, as a model for tumor growth, the limiting factors of the environment should be fairly constant in an individual, and hence growth proportionality to size is not as relevant in the model. For such a system the autonomous Gompertz model describes the system more correctly. In practice, such distinctions might not be very relevant for fitting and testing the Gompertz model against data; as the system constants are as unknown as the individual constants and all need to be estimated to fit the model to data. But as previously mentioned, the Gompertz model is not a very correct model for most scenarios. While most of the types of knowledge and intuition gained from working with the Gompertz model must therefore be regained for more advanced alternative models, the symmetries of the Gompertz model can be used with similar interpretations for other models, as long as the state has the same physical quantity. This is due to the ability to formulate characteristic symmetries of both the scalar models parameter independently. The motivation for using the parameter independence method is thus further strengthened.

All of the biological interpretations above relate to the matrix

$$\left(\partial_{(W,G)}\boldsymbol{J}\right)^{-1},$$

which in turn is only dependent on the invariants of the differential equations. There is therefore good reason to question whether symmetries are a useful way of investigating these types of biological properties of ODE:s. While the calculations in this thesis do not prove anything conclusively, approaches such as the one in chapter 5 to calculate invariants from reduced characteristics seems like a useful alternative when normal invariant calculations fail. Additionally, as seen for the structure of the Lotka–Volterra predator prey model, finding a function J consisting of functionally independent invariants is not always viable. In the case of the Lotka–Volterra model, the symmetry calculations lead to a partial construction of the general structure of the symmetries of the model, something that is not possible when using only the invariant theory, as the function $\partial_{(W,G)}\boldsymbol{J}$ is not fully known and therefore not invertible. Lastly, the symmetry generators are more intuitive for interpreting the symmetric properties than the basis of the reduced characteristic. Viewing the problem both from the perspective of symmetries and invariants of the differential equation is therefore preferable.

6.4 The future of symmetries for modeling in biology

As outlined in section 5.1, the possibilities for using symmetries in biological modeling is promising. If using symmetries turns out to be viable in even one of the cases presented, or another way relevant to researchers in biology, problems that so far have been impossible or too time consuming to solve might suddenly be approachable. The strength of using symmetries is that they relate to qualitative information about the systems studied, while most of the mathematical tools available in mathematical biology at the moment relate to quantitative information. Symmetries could therefore bridge the gap between established qualitative facts on the biological side of research and the mathematical models and simulations of those biological systems.

Common to all the uses for symmetries mentioned in this thesis is the need for the researcher to be able to find symmetries of a system. In this thesis only first order ODE:s were considered, and even in this case the calculations involved in finding symmetries grew to the scale were automation is needed, as seen in chapters 3 and 4. For most biological systems, ODE-models are simplifications of more sophisticated models that involve spatiality (and with that often higher order dynamics), randomness and time-delays. While the mathematics involved in finding symmetries for these more sophisticated models is far more complex than the theory covered in this thesis, the fact that the concept of symmetries can be generalized to most settings is a cause for optimism. The methods developed for determination of symmetries of ODE:s will thus have a good chance of being generalizable or at least have parallels when finding symmetries of more advanced systems.

As an example, the method of parameter independence developed in this thesis in chapter 4 solves problems in finding symmetries of first order ODE:s arising from the fact that the Lie algebras of the symmetries of first order ODE:s are infinite dimensional. But even for higher order differential equations, especially PDE:s, the problem of finding a general form for symmetry generators might not be viable to solve. The method of parameter independence could then be used to find general forms of at least all generators independent of some parameter in the same way as for first order ODE:s, as the method is compatible with the generalizations of the symmetry theory to higher order PDE:s. Similar results should be expected for many methods developed for some specialized subset of differential equations, which means that the study of symmetries of simplified biological models can act as a stepping stone to more robust methods. This indicates that there are good conditions for further research on symmetries in biological modeling along the directions outlined in this thesis.

Appendix A

Computer algebra system

For some of the larger calculations, a computer algebra system was used. This appendix contains an outline of the package developed in Python to make those calculations. The package is based on SymPy [35], and primarily adds tools relating to the trivial jet spaces encountered in this thesis, and the implementation and prolongation of infinitesimal generators. Three of the modules are described here. A fourth module, used for the visualizations in this thesis can be found along with the other three in the online repository available at https://github.com/Fexilus/MVEX60-Code.

`symmetries`

Calculate symmetries of ODE:s symbolically.

class `symmetries.Generator(xis, etas, total_space)`

A local coordinate representation of an infinitesimal generator.

Parameters:

- `xis (list[sympy.Expr])` - The base space components of the tangent field.
- `etas (list[sympy.Expr])` - The fiber components of the tangent field.
- `total_space (tuple[list[sympy.Expr], list["sympy.Expr"]])` - The base vectors of the total space on which the generator acts.

`__call__(expr, jet_space=None)`

Apply the generator on an expression on a jet space.

Parameters:

- `expr (sympy.Expr)` - The expression to apply the generator on.
- `jet_space (JetSpace, optional)` - The jet space in which the expression lives.

Returns: The expression after application of the generator.

Return type: `sympy.Expr`

`get_jet_space_basis(degree=0)`

Return the basis of a jet space on which the generator can act.
The ordering is the same as the ordering of `get_tangent_field()`.

Parameters:

`degree (int, optional)` - The degree of the jet space.

Returns: The expressions corresponding to the basis vectors of the jet space.

Return type: `list[sympy.Expr]`

`get_tangent_field(degree=0)`

Return the corresponding prolonged tangent field of the generator.
The ordering is the same as the ordering of `get_jet_space_basis()`.

Parameters:

`degree (int, optional)` - The degree of the prolongation.

Returns: The expressions corresponding to the components of the (possibly prolonged) tangent field.

Return type: `list[sympy.Expr]`

class `symmetries.JetSpace(base_coord, fiber_coord, degree)`

A local coordinate representation of a jet space.

Parameters:

`base_coord (list[sympy.Expr])` - The basis vectors of the base space.

`fiber_coord (list[sympy.Expr])` - The basis vectors of the fibers.

`degree (int)` - The degree of the created jet space. A degree of 0 corresponds to the total space.

`base_index(base_symbol)`

Returns the derivative index for a coordinate in the base space.

Parameters:

> `base_symbol` (**`sympy.Expr`**) - The symbol to find the base index of.

Returns: The multiindex of the desired symbol in the base space.

Return type: `tuple[int, ...]`

property `dependents`

The fibers of the total space on which the jet space is built.

Returns: The symbols of the original fibers.

Return type: `list[sympy.Expr]`

`extension(new_degree)`

Creates a jet space on the same total space of a higher degree.

Parameters:

> `new_degree` (**`int`**) - The degree of the extended jet space. Must be higher than the current degree.

Returns: A deep copy of the jet space, with additional jet fibers of higher degree.

Return type: **`JetSpace`**

property `original_total_space`

Return the coordinates of the total space on which the jet space is built

Returns: The coordinates of the base space and fiber.

Return type: `tuple[list[sympy.Expr], list[sympy.Expr]]`

`symmetries.decompose_generator(generator, basis)`

Decompose a generator by a basis of arbitrary constants or functions.
Only decomposition of generators linear in the basis is implemented.

Parameters:

> `generator` (**`Generator`**) - The generator to decompose.

`basis (list[sympy.Expr])` - The arbitrary constants or functions in which the generator can be decomposed.

Returns: The generators that span the space the input generator was in.

Return type: `list[Generator]`

`symmetries.generator_on(total_space)`

Returns a initialization method for generators on the total space.

Is meant to be used to reduce visual clutter in code where several generators on the same space are used.

Parameters:

`total_space (tuple[list[sympy.Expr], list[sympy.Expr]])` - The base vectors of the total space on which the generator acts.

Returns: A generator subclass without the total space argument in the initializer.

Return type: `Generator`

`symmetries.get_lin_symmetry_cond(diff_eqs, generator, jet_space, derivative_hints=None)`

Test if the linearized symmetry conditions hold differential equations.

Parameters:

`diff_eqs (sympy.Expr or list[sympy.Expr])` - The differential equation(s) expressed in jet space notation.

`generator (Generator)` - The generator corresponding to the Lie group of transformations to be tested.

`jet_space (JetSpace)` - The jet space on which the differential equations exist.

`derivative_hints (sympy.Expr or list[sympy.Expr])` - The highest order derivative(s) that the differential equation(s) can be solved for.

Returns: The differential equation(s) that must hold for the infinitesimal generator to generate a Lie group of symmetries. The differential equations are expressed in jet space notation.

Return type: `sympy.Expr or list[sympy.Expr]`

`symmetries.get_prolongations(xis, etas, jet_space)`

Calculate the coefficients of a vector field prolonged over a jet space.

The vector field is characterized by the coefficients of derivatives in the base space (xis) and the coefficients of derivatives in the fiber of the original fiber bundle (etas) from which the jet space is created.

Parameters:

- `xis (list[sympy.Expr])` - The base space components of the tangent field.
- `etas (list[sympy.Expr])` - The fiber components of the tangent field.
- `jet_space (JetSpace)` - The jet space on which the prolonged tangent field will be calculated.

Returns: The prolonged fiber expressions, ordered firstly by original fiber and secondly by corresponding derivative multiindex.

Return type: `dict[str, dict[tuple[int, ...], sympy.Expr]]`

`symmetries.lie_bracket(generator1, generator2)`

The Lie bracket of two generators in the same coordinate system.

Parameters:

- `generator1 (Generator)` - The left generator in the Lie bracket.
- `generator2 (Generator)` - The right generator in the Lie bracket.

Returns: The Lie bracket of the two generators.

Return type: `Generator`

`symmetries.total_derivative(jet_exp, coordinate, domain)`

The total derivative of an expression in a coordinate.

Parameters:

- `jet_exp (sympy.Expr)` - The expression to be derived.
- `coordinate (sympy.Expr)` - The coordinate to derive in. Should be one of the symbols of the base space.
- `domain (JetSpace)` - The jet space in which `jet_exp` exists.

Returns: The derived expression. This expression exists in the the (once) extended jet space compared to the domain of the derivative.

Return type: `sympy.Expr`

`symmetries.ansatz`

Make ansätze for generators.

`symmetries.ansatz.create_poly_ansatz(jet_space, degree=1)`

Create an infinitesimal generator that is polynomial in the components of a given jet space.

Parameters:

> `jet_space (JetSpace)` - The jet space on which the generator can act.
>
> `degree (int, optional)` - The degree of the polynomials in all generator components.

Returns: The generator and arbitrary constants defined by the ansatz.

Return type: `tuple[Generator, list[sympy.Expr]]`

`symmetries.utils`

Utilities for the main symmetries package.

`symmetries.utils.derivatives_sort_key(function_order=None, argument_order=None)`

Ad hoc sort key for derivatives.

Parameters:

> `function_order (list[sympy.Derivative], optional)` - An ordering of the functions.
>
> `argument_order (list[sympy.Expr], optional)` - An ordering of the arguments.

Returns: A sorting key for `sympy.Derivative` that sorts firstly by function, secondly by derivative degree and thirdly by derivative arguments.

`symmetries.utils.iter_wrapper(possible_iter)`

Ensures that the argument can be treated as an iterable.

Parameters:

> `possible_iter` - A possible iterable.

Returns: A guaranteed iterable.

`symmetries.utils.optional_iter(func)`

Decorator that allows the first argument and return value to be optionally treated as iterables.

Parameters:

`func` - The function should take an iterable as first argument and return an iterable.

Returns: The decorated function will accept either a single element or an iterable as first argument, and will return a single element or an iterable depending on the input type.

`symmetries.utils.replace_consts(exprs, new_const_name)`

Replace arbitrary constant from eg. `sympy.dsolve`.

Parameters:

`exprs (sympy.Expr or list[sympy.Expr])` - The expression(s) to replace constants in.

`new_const_name (str)` - The new base name to give to the constants. E.g. `new_const_name = r"\\alpha"` will result in constants `r"\alpha_{1}"`, `r"\alpha_{2}"` etc.

Returns: The new expressions and all the new constants.

Return type: `tuple[sympy.Expr or list[sympy.Expr], list[sympy.Expr]]`

`symmetries.utils.zip_strict(*iters)`

Zip two iterables and ensure that they are equal. Will be replaced with `strict=True` argument in Python 3.10.

Parameters:

`*iters` - Any number of iterables.

Returns: An iterable through tuples of the ingoing iterables.

Raises:

`ValueError` - if the iterables have different lengths.

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