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Competition Model

A Dynamic Approach to Product Sales Forecasting

Dr G.D. Jakubczik, Matthew Lettington, Dr Till Reichert
(mlt@jsc.de, gdj@jsc.de, trt@jsc.de)

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JSC at a Glance

- founded in 1991
- located in Eltville (near Wiesbaden), Germany
- independent

- partner network for turnkey solutions

- ~15 senior and management consultants
- multi-disciplinary team
- (chemist, pharmacist, physician, economists, mathematicians, it professionals)

- focus on chemicals, life science products, (fast moving) consumer goods

- team oriented and customer focused approach
- dedicated to quality and striving for first class results
- fact driven and application of sound methodologies

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Overview

The presentation encompasses aspects of our recent research and achieved results in forecasting the Pharmaceutical Market.

1. Introduction
2. Model Theory
   - 2.1 Logistic Growth Model
   - 2.2 Two Species Models
   - 2.3 Generalized LV Competition Models
3. Case Study “Respiratory Market”
   - 3.1 Methodology
   - 3.2 Results
   - 3.3 Scenario
4. Assessment
5. Outlook

Appendix

1. Introduction

1.1 Objectives

The fundamental objectives behind our continuous research are:

- To find predictive modelling techniques for forecasting of market shares and product sales.
- To allow for product interaction and competition dynamics.
- To adapt and apply these techniques to specific therapeutic areas in the Pharmaceutical Market.
- To include conformity to historic data for model validation.
- To allow for application of multiple scenarios and simulation of outcome.

1. Introduction

1.2 Market Description (i)

The pharmaceutical market is worth about $690 billion (2007). Up to ten years, boundary conditions for many segments of the market are quite stable.

- Incidence and prevalence of diseases are relatively well known.
- Guidelines for product approval by authorities are well established.
- Launch of generics is determined by loss of exclusivity (patent expiry).
- Patent expiry of major products can change market shares of individual products but not necessarily treatment patterns.
- New product but established therapeutic class needs ~10 years prior to market launch (last years are visible).
- Competition dynamics among products of same class is highly influenced by exploitation of partial advantages and sales efforts.

1. Introduction

1.2 Market Description (ii)

Uncertainties emerge when true innovations are expected in the forecasting period or when the economic situation deteriorates significantly.

- New mode of action (“true innovation”) has latency period of more than 15 years.
- Disruptive technologies (e.g. stem cell therapy, gene therapy) might emerge - but lead time is greater than 30 years.
- New regulatory hurdles might be erected (e.g. companion diagnostics).
- General economic situation drives cost containment and cost cutting measures.
- Structural changes in healthcare organization impacts market access (pricing and reimbursement).

1. Introduction

1.3 Model Selection (i)

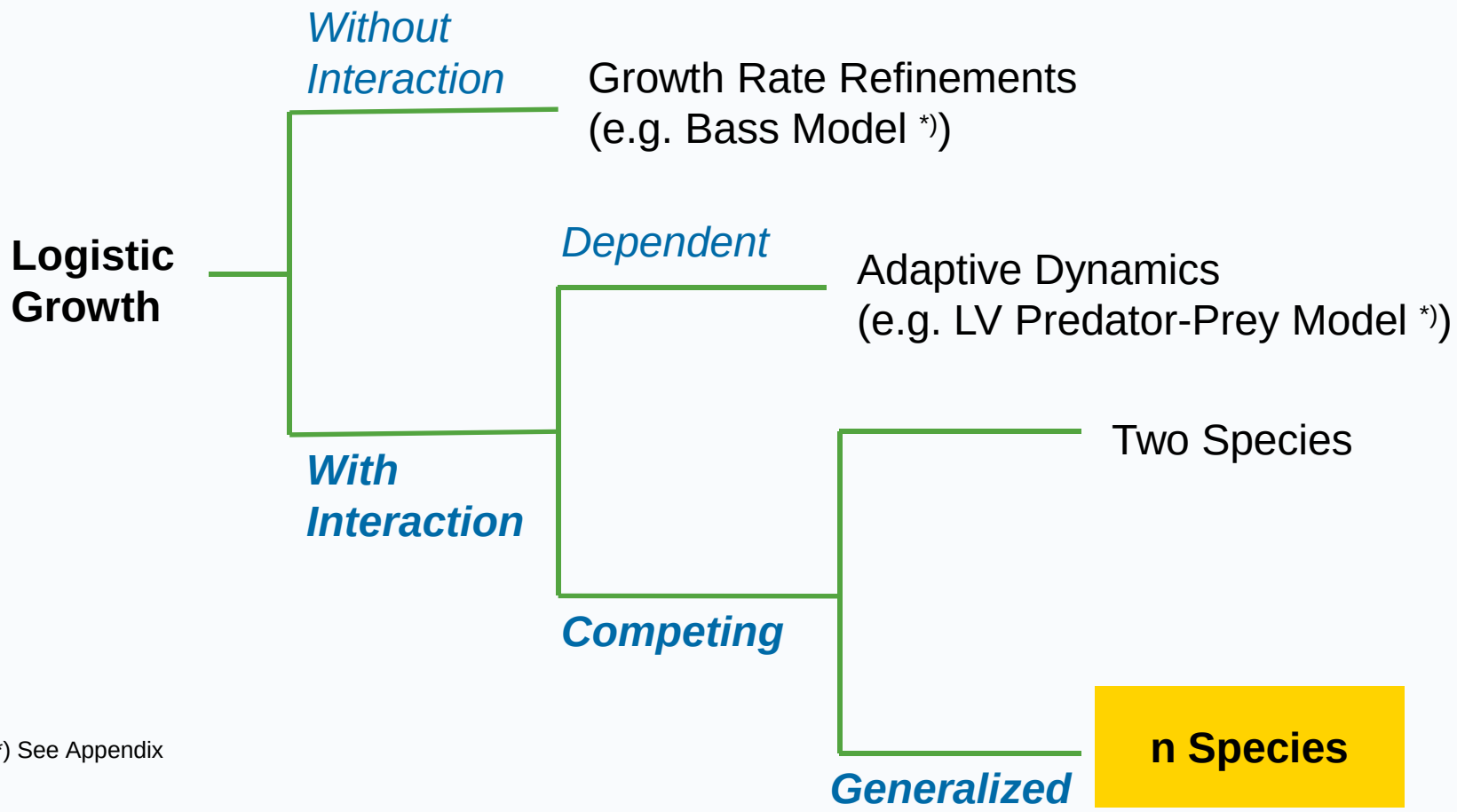
There exist a number of established modelling approaches. For our purpose, growth models are suitable as they allow for competition and automated trials.

- Time Series Analysis (Pure Statistics) – can use sophisticated techniques such as Single Spectrum Analysis (SSA) or Autoregressive Integrated Moving Average (ARIMA) to differentiate between inherent patterns within the data and perceived noise.
- Simulation (Imitation) – techniques range from physical constructions to pure software simulations. Results can be very accurate when all fundamental parameters are known.
- Growth and Diffusion (Dynamics) – methods can be complex and encompass a variety of non-linear techniques, to include interaction, dependence and competition.

1. Introduction

1.3 Model Selection (ii)

Within the general category of growth models we focus on the n-dimensional LV model, which is based on n species competing for a common source.



*) See Appendix

2. Model Theory

2.1 Logistic Growth Model

The logistic population growth model (*Verlhurst 1844)* defines the net birth rate (i.e. birth – death) of a population *P* at time *t.*

Differential Equation

$$\frac{dP}{dt} = F(P,M)P = f\left(1 - \frac{P}{M}\right)P.$$

M = carrying capacity.
F(P,M) = fractional growth rate, $0 \leq F(P,M) \leq 1$.
f = maximum fractional growth rate, $F(P,M) \leq f \leq 1$

Explicit Solution

$$P(t) = \frac{M}{(M/P_0 - 1)\,e^{-ft} + 1}$$

fP contributes standard first-order linear positive feedback.
$-fP^2 / M$ contributes non-linear negative feedback.

2. Model Theory

2.2 Two Species Models

When considering a two-dimensional system there is often an interaction. The competition model (Lotka 1924) is shown below.

Differential Equation

$$\frac{dP_1}{dt} = (f_1 - g_1 P_1 - \alpha_{1,2} P_2) P_1 \quad \Rightarrow \quad = f_1 \left(1 - \frac{P_1}{M_1} - \frac{\beta_{1,2}}{M_1} P_2\right) P_1,$$

$$\frac{dP_2}{dt} = (f_2 - \alpha_{2,1} P_1 - g_2 P_2) P_2 \quad \Rightarrow \quad = f_2 \left(1 - \frac{\beta_{2,1}}{M_2} P_1 - \frac{P_2}{M_2}\right) P_2.$$

P_1 per-capita growth rate = $f_1 - g_1 P_1 - \alpha_{1,2} P_2$, where $f_1, f_2, g_1, g_2, \alpha_{1,2}, \alpha_{2,1} > 0$, and

f_1 is the natural or isolated growth rate
$- g_1 P_1$ is the *intra*-species competition
$\alpha_{1,2} P_2$ is the *inter*-species competition

Similar interpretations apply for P_2

2. Model Theory

2.3 Generalized LV Competition Equations

For n species, we now assume that $f_i = 1$, $1 \le i \le n$, and generalize the equations.

Differential Equation

$$\frac{dP_i}{dt} = \left(1 - \sum_{j=1}^{n} \frac{\beta_{i,,j}}{M_i} P_j\right) P_i .$$

For further simplification we also assume that $\beta_{i,i} = M_i$, $1 \le i \le n$, so that

Simplified Differential Equation

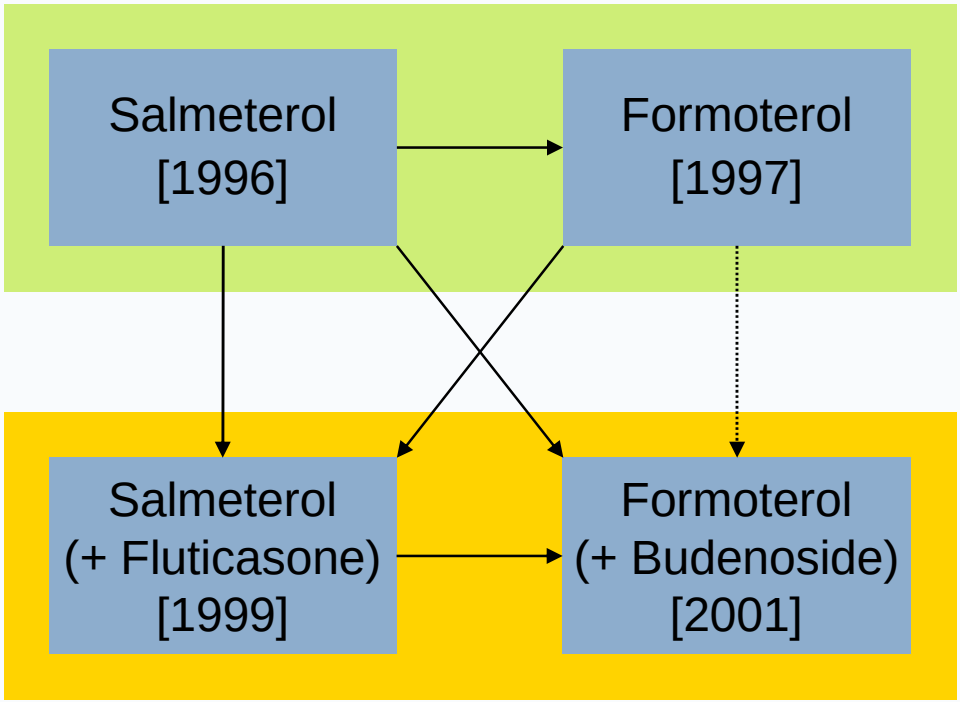
$$\frac{dP_i}{dt} = \left(1 - P_i - \sum_{\substack{j=1 \\ j \ne i}}^{n} \alpha_{i,j} P_j\right) P_i .$$

This ensures that $0 \le P_i \le 1$, $1 \le i \le n$.

3. Case Study

3.1 Methodology – Universe

In our case study, we investigate a selected class in the (German) respiratory market. The relevant molecules compete for share in this quite stable market.



Long-Acting
Beta-Agonists – LABA
(Mono Products)

LABA + ICS
(Combo Products)

[year] launch year in German respiratory market; ⟶ net change of DDDs

3. Case Study

3.1 Methodology – Data

We obtain historic data for the German respiratory market segment from a publicly available source*) using the same approach since more than 20 years.

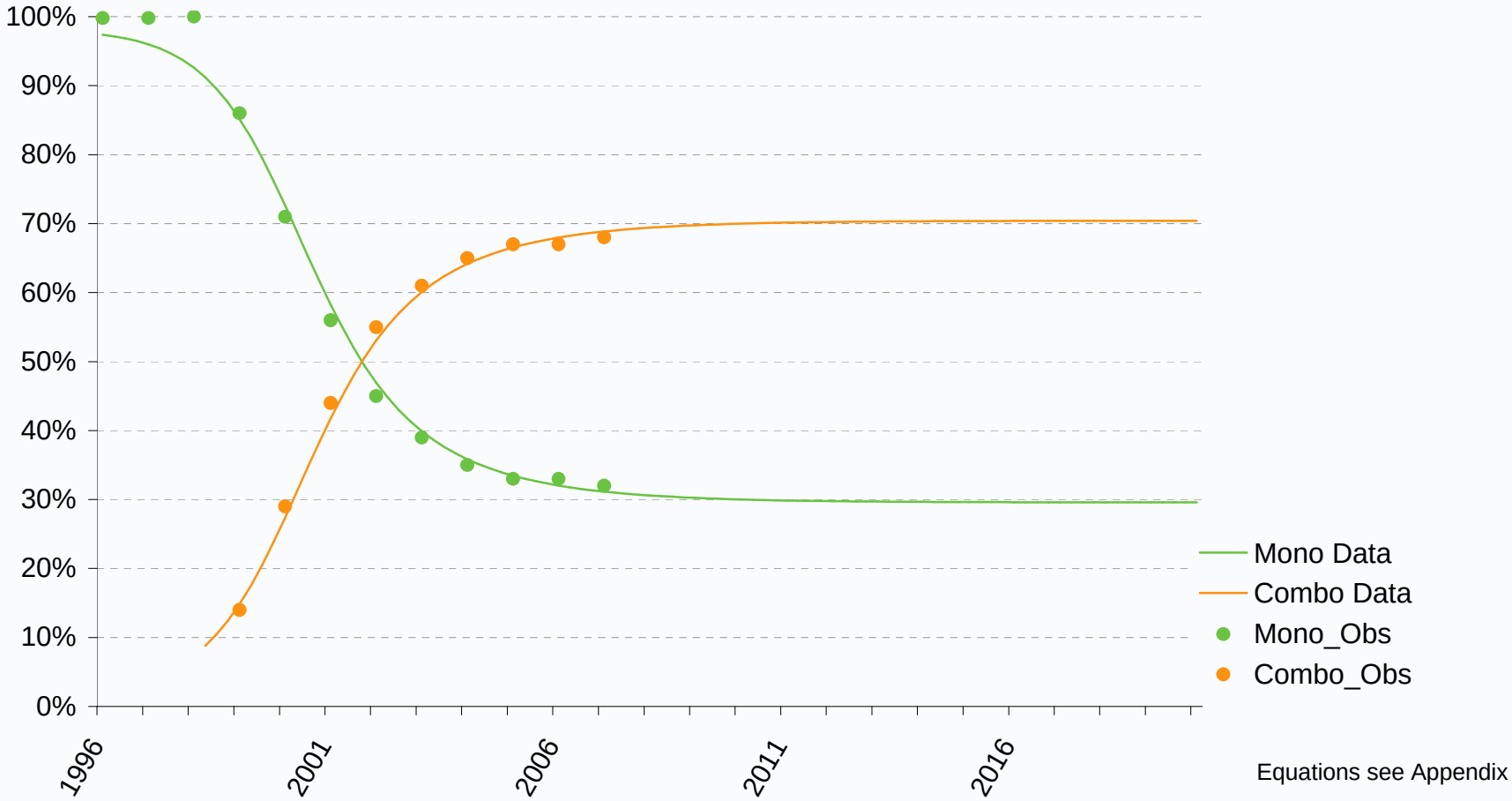
- The data is collated into defined daily doses (DDD's) per molecule per annum and recorded as a market share fraction.**)
- Competition systems of differential equations are "fitted" to the data by molecule (with parameter limitations).
- The current "fit process" uses aggregate variance methods.
- The resulting system can be used to design scenarios and to forecast future DDD development.
- The DDD forecast figures can be converted into sales figures using historic price evolution and assumptions for the future.

*) Arzneiverordnungs-Reports 1991-2008
**) See Appendix

3. Case Study

3.2 Results – Top View

In a first step the interaction between LABA mono products and combo products is investigated.

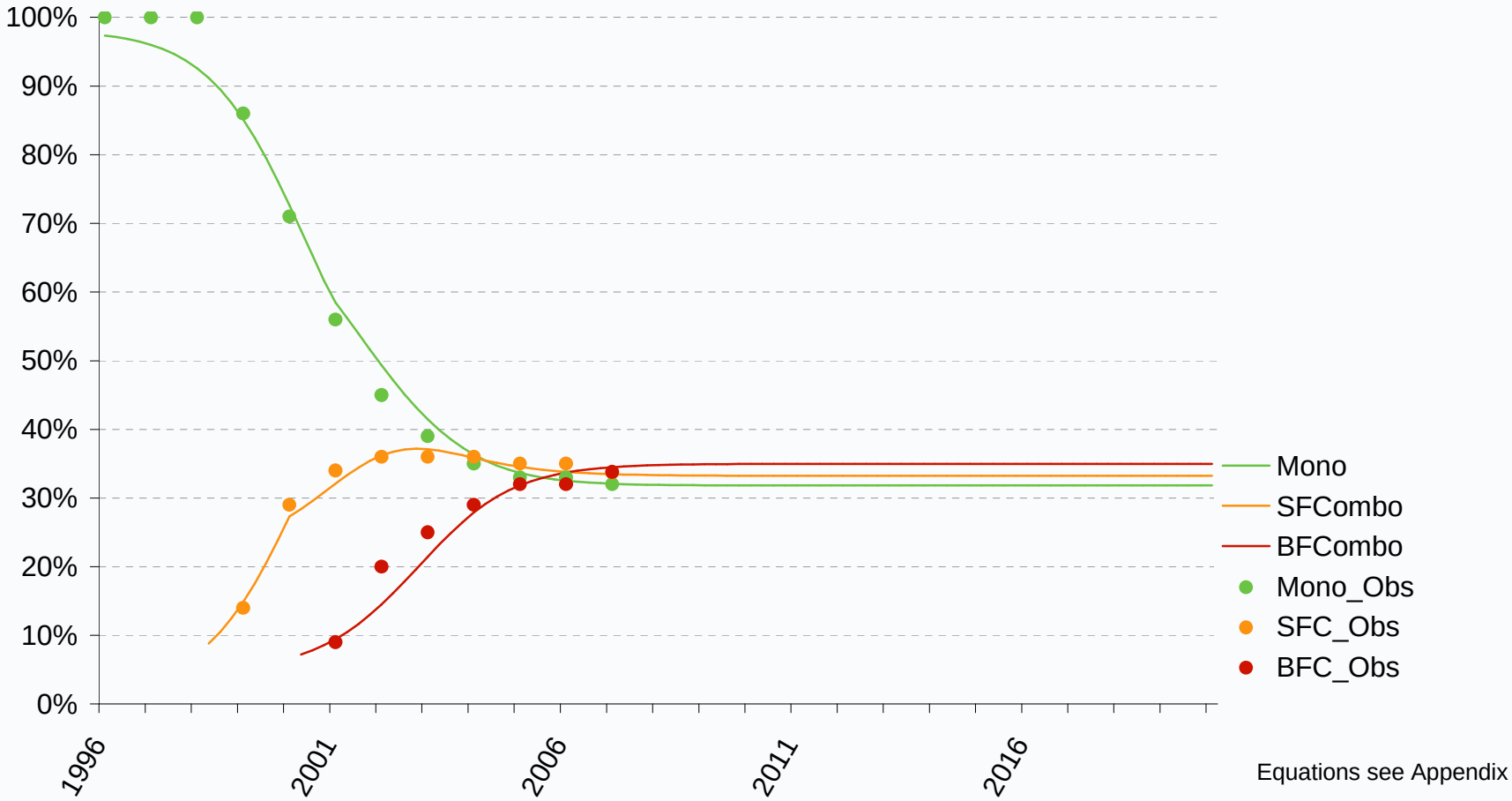


Equations see Appendix

3. Case Study

3.2 Results – Three-Dimensional System Graphs

In a second step, a more detailed model for the two Combos is developed.

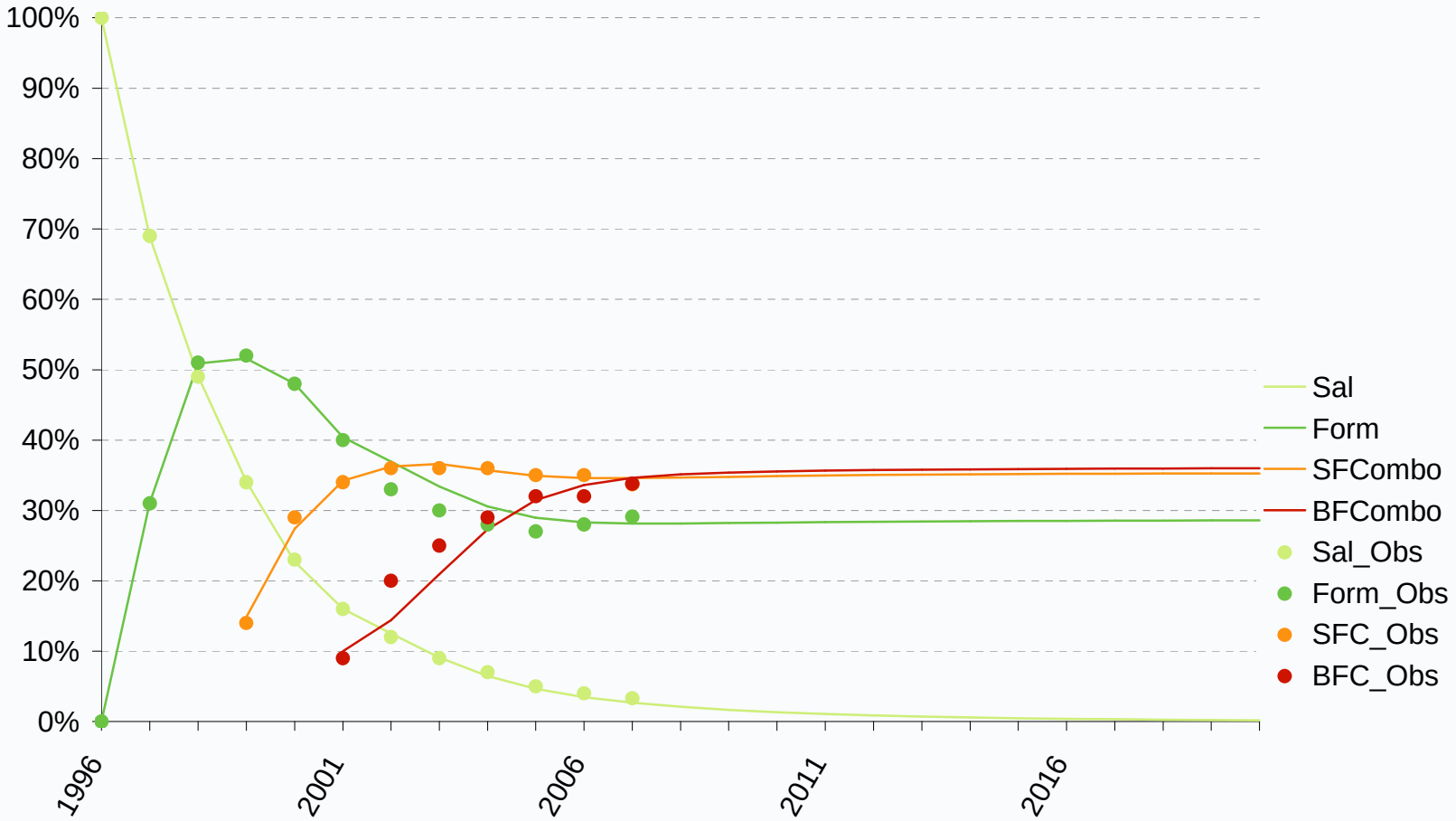


Equations see Appendix

3. Case Study

3.2 Results – Four-Dimensional System Graphs

In the third modelling step all molecules (and combinations) are taken into consideration.



3. Case Study

3.2 Results – Four-Dimensional System Equations

We “best fit” a four-dimensional system of differential equations to Salmeterol, Formoterol, SFCombo and BFCombo data.

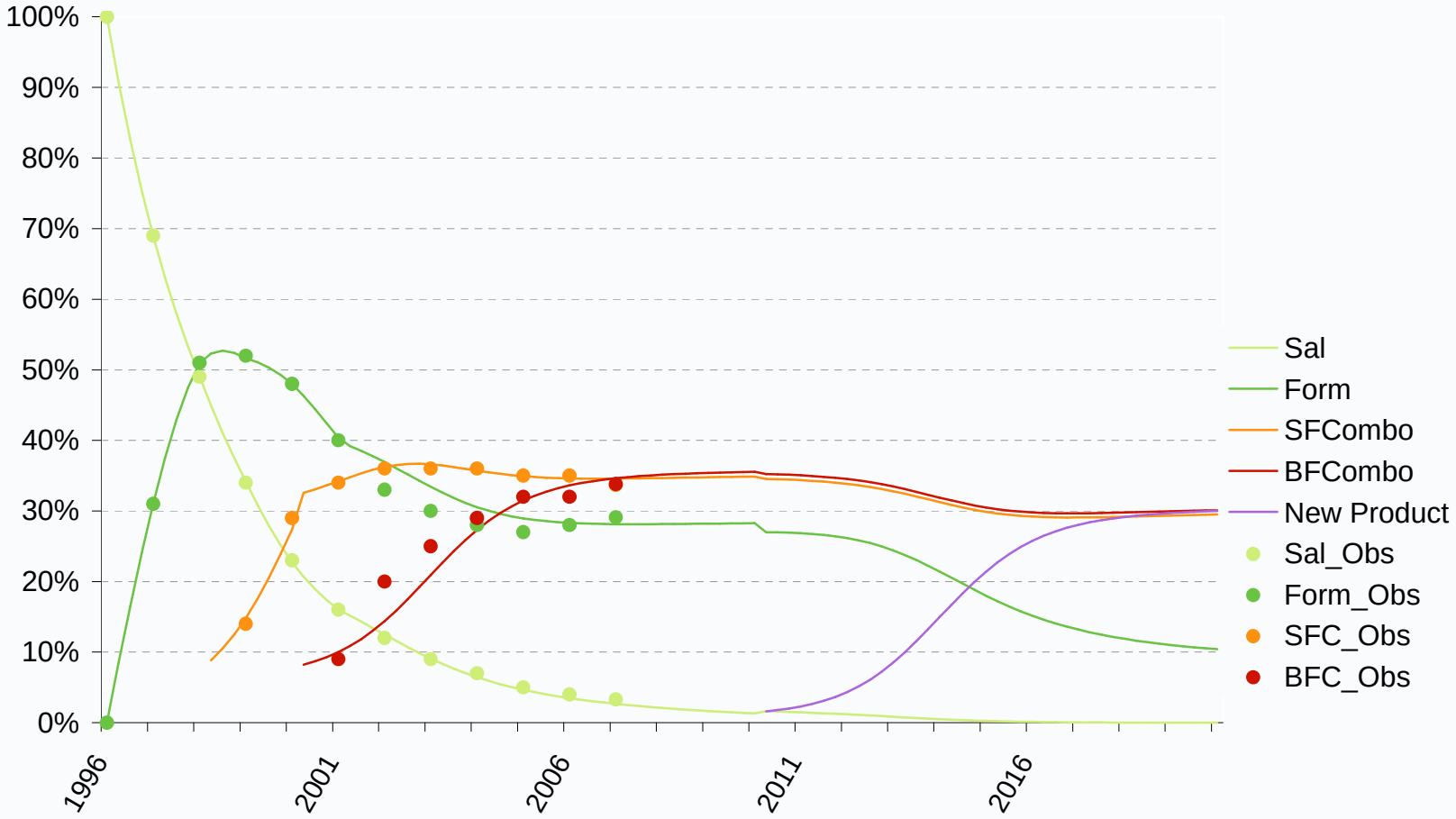
Differential Equation

- *Salmeterol* (=V) $\frac{dV}{dt} = (1 - V - 0.89W - 0.21X - 0.27Y)\,V$
- *Formoterol* (=W) $\frac{dW}{dt} = (1 - W - 0.21X)\,W$
- *SFCombo* (=X) $\frac{dX}{dt} = (1 - X - 0.02Y)\,Y$
- *BFCombo* (=Y) $\frac{dY}{dt} = (1 - Y)\,Y$

3. Case Study

3.3 Scenario – Five-Dimensional System Graphs

The impact of a new LABA molecule (QD mono product, assumed launch in 2011) on the current system is investigated.



3. Case Study

3.3 Scenario – Five-Dimensional System Equations

The new product and the respective interaction coefficients are introduced manually to the established four-dimensional system.

Differential Equation

- *Salmeterol* (=V) $\frac{dV}{dt} = (1 - V - 0.89W - 0.21X - 0.27Y - Z)\,V$
- *Formoterol* (=W) $\frac{dW}{dt} = (1 - W - 0.21X - 0.5Z)\,W$
- *SFCombo* (=X) $\frac{dX}{dt} = (1 - X - 0.02Y)\,Y$
- *BFCombo* (=Y) $\frac{dY}{dt} = (1 - Y)\,Y$
- *New Product* (=Z) $\frac{dZ}{dt} = (1 - Z)\,Z$

4. Assessment

4.1 Model Validation

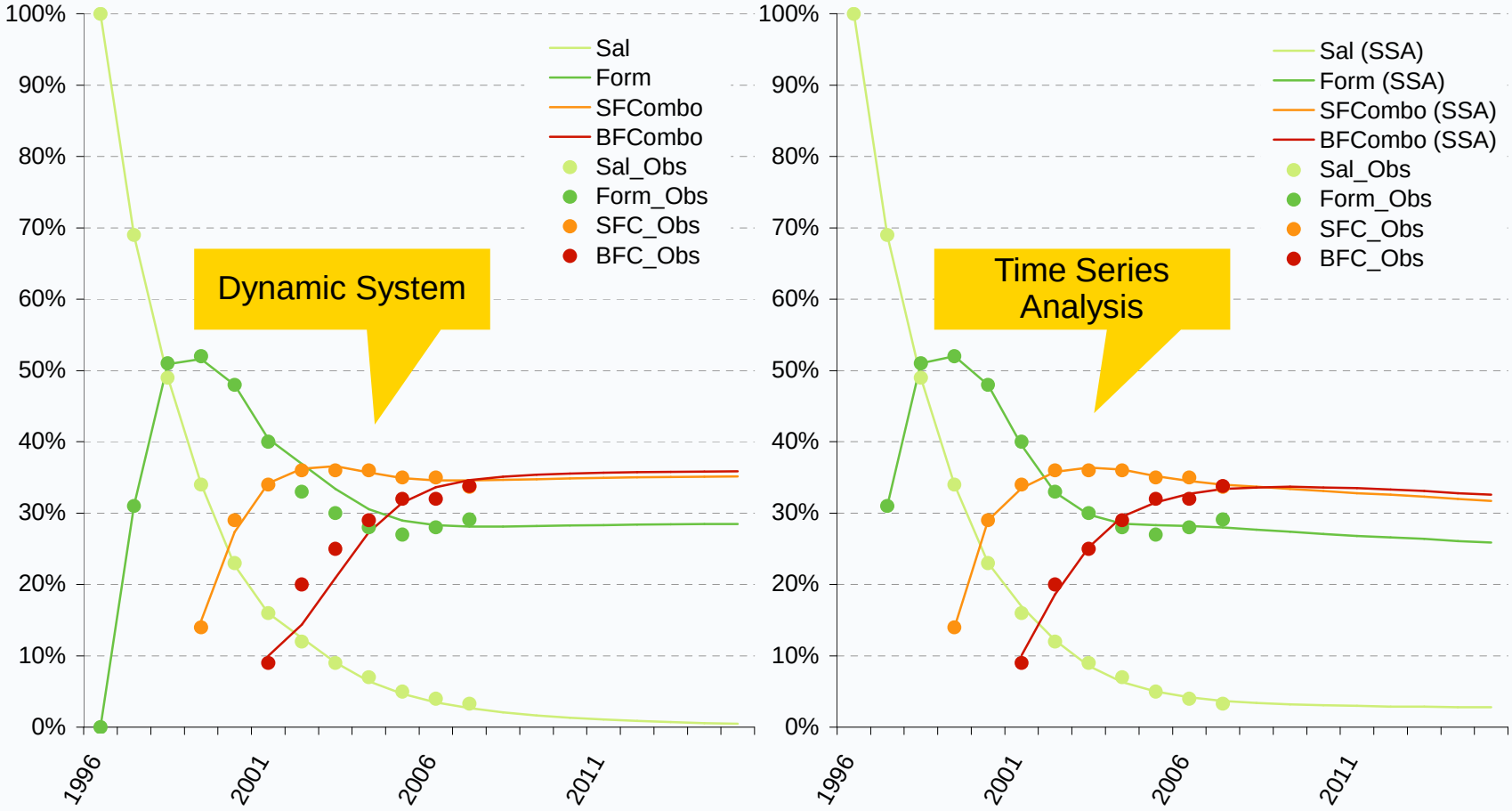
State-of-the-art Time Series Analysis has been used for model validation.

- Validity of a forecast is strengthened when different methodologies concur.
- We compare our forecast results with those obtained using the Time Series Analysis (CaterpillarSSA) method.
- Both forecasts are consistent, which adds weight to the suitability of our selected approach (see graphs).
- The LV model exhibits some limitations to represent the early launch period of a product properly (steep uptake curves).
- The ability to analyze scenarios is a key point when considering which forecasting technique to use.
- Time Series Analysis is “model free” and scenario development for future events is very limited.
- With variation of interaction coefficients, the investigation of impact of future events in the Dynamic System model is very convenient.

4. Assessment

4.2 Comparison Time Series Analysis

The results obtained using both the dynamic systems (LV) and time series analysis (CaterpillarSSA) are consistent.



4. Assessment

4.3 Final Conclusions

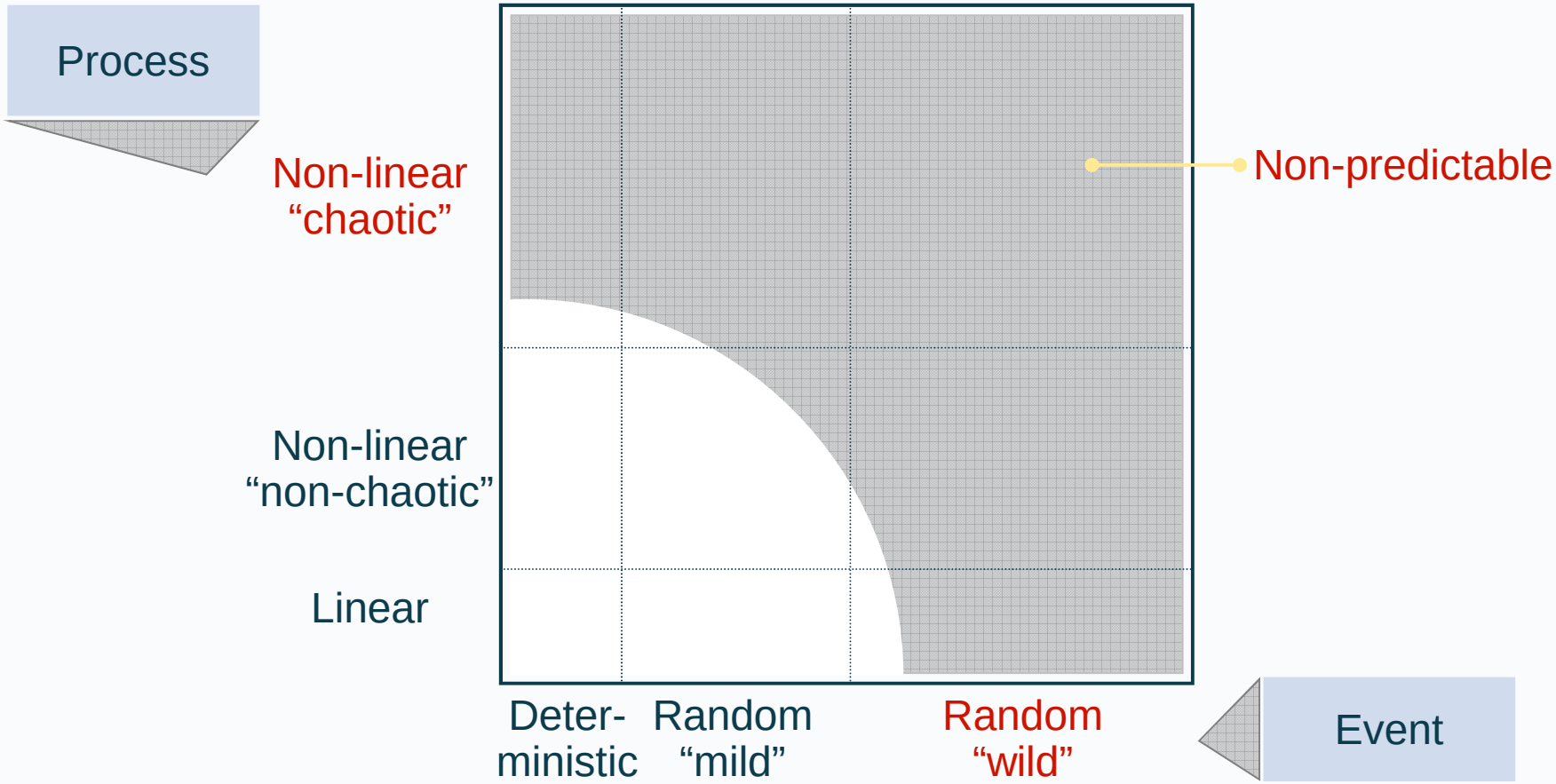
Achieved results suggest the suitability of the selected approach to model complex market conditions (forecast horizon > 5 years).

- The generalized LV Competition Equations can be applied for segments of the pharmaceutical market with stable boundary conditions.
- Different levels of detail deliver consistent (scaleable) results (combined DDD market share for Combos in all models).
- The model has been validated with state-of-the-art time series analysis software.
- The methodology can be used to predict market shares (or equivalents) and sales (see also Appendix).
- Paramount advantage is that the impact of new entrance in a given system can be calculated comfortably – comparison of multiple scenarios is possible.
- Limitations might occur when disruptive technologies emerge and the fundamental market framework is changed.

5. Outlook

5.1 Limitations in Predictability

We cannot predict the future. Characteristics of complex systems impede long-term planning efforts. We have to work with scenarios.



5. Outlook

5.2 Areas for Expansion

Next steps will be taken mainly in two directions: Technical extensions for scenario evaluation and inclusion of random elements.

- Further modelling to encompass all likely scenarios.
- Expansion of the model to include elements of randomness.
- Development of a repository with interaction coefficients (influence of profile, sequence in market, price etc.) will be helpful for the scenario design (launch of new products, generics etc.).
- Possible incorporation of other statistical optimization processes.
- Further development of the model may include individual growth rates and carrying capacities.

Appendix
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Appendix
Bass Model

The logistic model has appeared in a number of guises and was adapted by Bass (1969) to model the diffusion of innovations.

Explicit Solution (adapted)

$$P(t) = \frac{M}{(M / P_0 - 1)\, e^{-ft} + 1}$$

$$P(t) = f(t)\, M = \frac{M\,(1 - e^{-(p+q)t})}{1 - (q/p)\, e^{-(p+q)t}}$$

M = target population

$P(t)$ = purchases at time t

$f(t)$ = fraction of M at time that have adopted new product

p = coefficient of intrinsic tendency to adopt

q = coefficient of extrinsic tendency to adopt

Averages of p and q are around 0.03 and 0.38 respectively.

Appendix
Predator-Prey Model

When considering a two-dimensional system there is often an interaction. A classic example is the Lotka-Volterra predator-prey model.

Differential Equations

$$\frac{dP_1}{dt} = (f_1 - g_1 P_2) P_1 \qquad \frac{dP_2}{dt} = (-f_2 + g_2 P_1) P_2, \qquad f_1, f_2, g_1, g_2 > 0.$$

P_1 = prey population

P_2 = predator population

In terms of per-capita growth we have:

f_1 = growth of P_1 in absence of predators
- $g_1 P_2$ = losses of P_1 to predators
- f_2 = decrease in P_2 if no prey to eat
$g_2 P_1$ = growth of P_2 due to hunting

Appendix
Data Tables

MARKET TABLE BY MOLECULE DDD (MILLIONS) P.A.

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Salmeterol	19,6	28,6	33,3	33,5	28,8	26,7	23,8	21,0	16,8	14,8	12,4	10,3
Formoterol	0,0	12,9	34,5	50,7	60,8	67,4	68,1	70,3	69,1	77,5	83,9	90,3
S+F Combo	0,0	0,0	0,0	14,0	37,1	57,0	73,1	82,5	87,2	100,5	103,3	104,4
B+F Combo	0,0	0,0	0,0	0,0	0,0	15,7	40,7	57,5	71,6	90,8	95,9	104,8
TOTAL	**19,6**	**41,5**	**67,8**	**98,2**	**126,7**	**166,8**	**205,7**	**231,3**	**244,7**	**283,6**	**295,5**	**309,8**

TABLE OF MARKET FRACTION BY MOLECULE P.A.

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Salmeterol	1,000	0,689	0,491	0,341	0,227	0,160	0,116	0,091	0,069	0,052	0,042	0,033
Formoterol	0,000	0,311	0,509	0,516	0,480	0,404	0,331	0,304	0,282	0,273	0,284	0,291
S+F Combo	0,000	0,000	0,000	0,143	0,293	0,342	0,355	0,357	0,356	0,354	0,350	0,337
B+F Combo	0,000	0,000	0,000	0,000	0,000	0,094	0,198	0,249	0,293	0,320	0,325	0,338
TOTAL	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**	**1,00**
						-						
Mono	1,00	1,00	1,00	0,86	0,71	0,56	0,45	0,39	0,35	0,33	0,33	0,32
Combo	0,00	0,00	0,00	0,14	0,29	0,44	0,55	0,61	0,65	0,67	0,67	0,68

Source: Arzneiverordnungs-Reports 1996-2008

Appendix

Results – Two-Dimensional System Equations

We “best fit” a two-dimensional system of differential equations to Mono and Combo data.

Differential Equations

- *Mono* (=V) $$\frac{dV}{dt} = (1 - V - 0.58X)\,V$$
- *Combo* (=X) $$\frac{dX}{dt} = (1 - X)\,X$$

Appendix

Results – Three-Dimensional System Equations

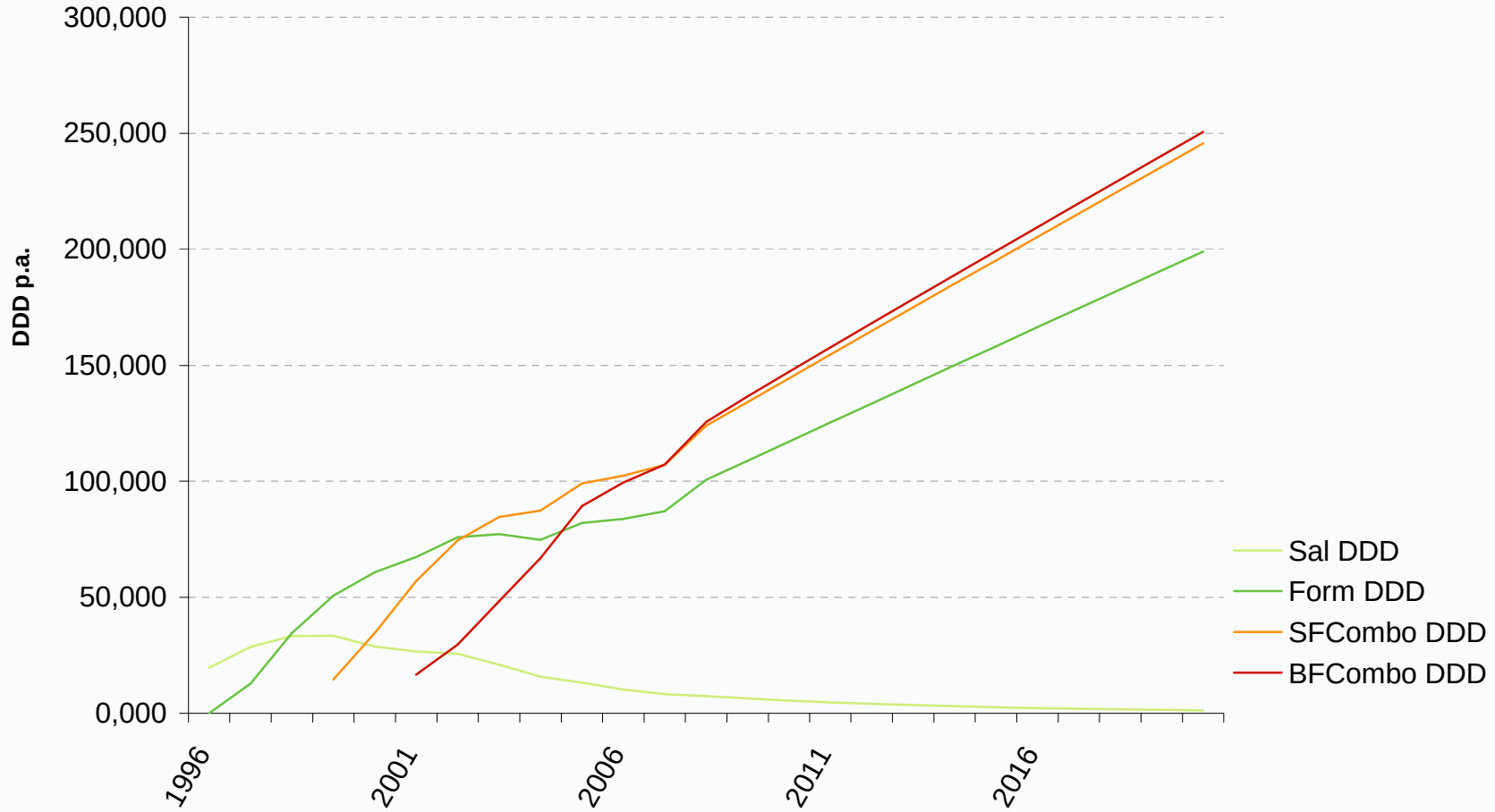
We “best fit” a three-dimensional system of differential equations to Mono, SFCombo and BFCombo data.

Differential Equations

- *Mono* (=V) $\frac{dV}{dt} = (1 - V - 0.95X)V$
- *SFCombo* (=X) $\frac{dX}{dt} = (1 - X - 0.05Y)X$
- *BFCombo* (=Y) $\frac{dY}{dt} = (1 - Y)Y$

Appendix
DDD Development

Using linear regression we obtain the LABA Defined Daily Dose market forecast and multiply this by market shares obtained from the 4D-model.



Thank you for your attention!