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OPTIMIZATION APPLIED ON REGULATORY AND ECO-FINANCE NETWORKS – SURVEY AND NEW DEVELOPMENTS –

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In Memory of Our Dear Teacher and Friend Professor Alexander Rubinov

Abstract: In this paper we survey recent advances and mathematical foundations of regulatory networks. We explain their interdisciplinary implications with special regard to Operational Research and financial sciences and introduce the so-called *eco-finance networks*. These networks, originally developed in the context of modeling and prediction of gene-expression patterns, have proved to provide a conceptual framework for the modeling of dynamical systems with respect to errors and uncertainty as well as the influence of certain environmental items. Given the noise-prone measurement data we extract nonlinear differential equations to describe and investigate the interactions and regulating effects between the data items of interest and the environmental items. In particular, these equations reflect data uncertainty by the use of interval arithmetics and comprise unknown parameters resulting in a wide variety of the model. For an identification of these parameters Chebychev approximation and generalized semi-infinite optimization are applied. In addition, the time-discrete counterparts of the nonlinear equations are introduced and their parametrical stability is investigated by a combinatorial algorithm which detects the region of parameter stability. We analyze the structural stability of the regulatory networks, we discuss a modeling by stochastic differential equations and explain how spline regression applied in an additive model could be integrated into our analysis. We conclude with two examples for eco-finance networks in the fields of CO_2-emissions-control and portfolio optimization for natural gas transportation systems.

Key words: *regulatory networks, gene-environment-networks, eco-finance-networks, uncertainty, generalized semi-infinite programming, stochastic differential equations, spline regression*

Mathematics Subject Classification: *93A30, 92D10, 90C34*

1 Introduction

In the last decade, the mathematical analysis of highly interconnected systems has become increasingly important as the development of high-throughput technologies resulted in an accelerated generation of massive quantities of financial, technical, environmental and biological data. The availability of large data sets now allows to gain deeper insights in the dynamic behaviour of complex systems and opens promising avenues for further scientific progress. These systems often involve two different kinds of data sets in form of certain *key* or *target variables* and additional *environmental variables*. For a deeper analysis one has to describe and investigate the interactions and regulating effects between data items of interest

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and the environmental items, encoded in the *regulatory-network*. As these models are based on real-world data, errors and uncertainty have to be considered. In this paper we present various kinds of inter-regulated models under uncertainty, we investigate their dynamics and analyze their stability behaviour. In addition, we present some recent approaches based on stochastic differential equations and additive regression models. Finally, we explain the interdisciplinary implications in finance, technology and Operational Research and introduce the so-called *Eco-Finance-Networks*.

2 The General Model

A first and quite general model for complex two-class-systems is given by the time-continuous system

$$\dot{\mathbb{X}} = \mathbb{F}(\mathbb{X}),$$

where the time-dependent d-vector $\mathbb{X} = (\mathbb{X}_1, \ldots, \mathbb{X}_n, \mathbb{X}_{n+1}, \ldots, \mathbb{X}_{n+m})^T$ comprises the n levels of the *target variables* and the values of the m environmental factors. The continuous change in the data is represented by $\dot{\mathbb{X}} (= \frac{d\mathbb{X}}{dt})$, and $\mathbb{F} : \mathbb{R}^d \to \mathbb{R}^d$ is composed of nonlinear coordinate functions $\mathbb{F}_i : \mathbb{R}^d \to \mathbb{R}$ $(i = 1, 2, \ldots, d = n+m)$ (cf. [10, 22, 41, 53, 62] for different dimensions). As the nonlinear function $\mathbb{F}$ in the time-continuous system is determined by unknown parameters we have to deal with parameter identification based on noise-prone data vectors obtained from measurements $\bar{\mathbb{X}}^\kappa$ $(\kappa = 0, 1, \ldots, l)$.

Example:

(i) The models under consideration have been developed in the context of the analysis and prediction of gene-expression patterns [54, 60, 61, 62, 63, 64, 65, 66, 69]. In this *gene-environment networks* the target variables represent the expression levels of the n genes, whereas the m environmental items stand for external factors (e.g., transscription factors, toxins or radiation).

(ii) In Section 13 we introduce the *eco-finance networks* and apply them to an example from Operational Research. In [36, 60, 62] the *Technology-Emissions-Means Model* (in short: *TEM-model*) has been investigated, which allows a simulation of the cooperative economic behaviour of countries/enterprises with the aim of a reduction of CO_2-emissions. Here, the target variables are the emissions that the actors wish to reduce and the required financial means act as additional environmental items.

3 Errors and Uncertainty

For a representation of measurement errors and uncertainty we integrate interval arithmetics into our modelling [11, 14, 31, 32, 40, 42]. The levels of the target and environmental items are given by

$$\mathbb{X}_i = \bar{\mathbb{X}}_i \pm \mathrm{Err}_i \quad (i = 1, 2, \ldots, d),$$

where $\mathrm{Err}_i > 0$ denotes the maximal error to be made at the measurements of the variable $\mathbb{X}_i$ [54]. This measurement error leads us to assume that the state $\mathbb{X}_i$ has to lie in the interval $[\bar{\mathbb{X}}_i - \mathrm{Err}_i, \bar{\mathbb{X}}_i + \mathrm{Err}_i]$ and, hence, the state vector $\mathbb{X} = (\mathbb{X}_1, \mathbb{X}_2, \ldots, \mathbb{X}_d)^T$ has to be in the parallelpipe

$$\prod_{i=1}^{d} \left[\bar{\mathbb{X}}_i - \mathrm{Err}_i, \bar{\mathbb{X}}_i + \mathrm{Err}_i\right].$$

Here, we can speak of confidence intervals and a confidence parallelpipe. Those parallelpipes and intervals usually come from a perspective where functional dependencies among any two of the errors made in the measurements of the variables $\mathbb{X}_i$ are not taken into account explicitly. Moreover, they are usually smaller than the ellipsoides and their orthogonal projections into the 2-dimensional Cartesian planes, respectively. Indeed, those confidence ellipsoids are obtained with respect to stochastic dependencies of the error variables. Those dependencies are the case in reality, e.g., in financial studies and in microarray experiments as well. In reverse, any ellipsoid can be inscribed into a sufficiently large parallelpipe which, in addition, could be suitably located and directed in space around its eigenaxes. According to his/her experience and wish for confidence (trust region), the modeler can enforce a certain size of the parallelpipe by additional constraints on the interval limits, which are the variables in our parameter estimation. We underline that a direct modeling based on *ellipsoidal calculus* [29] and corresponding parameters is possible, too. This approach will be discussed in a forthcoming paper.

4 Regulatory Networks

The dynamic interaction between the n target variables (without any environmental items) can be modelled by a system of continuous differential equations

$$(\mathcal{CE})_{\text{target}} \quad \dot{X} = A(X)X,$$

where the (interval) matrix A may depend on the vector $X = (\mathbb{X}_1, \mathbb{X}_2, \ldots, \mathbb{X}_n)^T$ of target variables (cf. [54, 65]). From this equation we obtain the following discrete-time equation and dynamics

$$(\mathcal{DE})_{\text{target}} \quad X^{(k+1)} = A^{(k)}X^{(k)} \ \ (k \in \mathbb{N}_0),$$

where the $A^{(k)}$ can be taken as interval matrices and the stability can be investigated by Brayton and Tong's algorithm [1, 65]. In order to include environmental items into our continuous model under the presence of noise and uncertainty we extended in [53, 54, 65] the model from [17, 20] and provided the continuous equation

$$(\mathcal{CE}) \qquad \dot{\mathbb{X}} = \mathbb{A}(\mathbb{X})\mathbb{X}, \quad \mathbb{X}(t_0) = \mathbb{X}^{(0)}.$$

The system matrix $\mathbb{A}(\mathbb{X})$ is a $(d \times d)$-matrix whose entries are intervals, defined by a family of functions which include unknown parameters. In this way, we can integrate uncertainty with respect to the interactions between the target variables, to the effects between the environment and the target variables, or between environmental items. The initial value $\mathbb{X}^{(0)}$ in $(\mathcal{CE})$ consists of the interval-valued levels obtained by the first measurement $\bar{\mathbb{X}}(t_0) = \bar{\mathbb{X}}^{(0)}$. As this may result in a large and highly interconnected network we will later on restrict on an approximate model and network. For this we will improve our model by imposing bounds on the admissible number of regulating effects exercised per target item and also on the effects of the environment onto the target variables.

5 Identification and Stability

When we look at the parameterized entries of the continuous model $(\mathcal{CE})$ we have to examine the respective *optimization* and must provide a *stability analysis*. We note that both issues lead to *bilevel problems*. In case of optimization we have to deal with the problem $\min_y \sum_{\kappa=0}^{l-1} \left\| \mathbb{A}_y\big(\bar{\mathbb{X}}^{(\kappa)}\big)\bar{\mathbb{X}}^{(\kappa)} - \dot{\bar{\mathbb{X}}}^{(\kappa)} \right\|_\infty^2$ and by this with approximation based on squared errors.

Here, the vector y comprises a subset of all the parameters and the vector $\dot{\bar{\mathbb{X}}}^{(\kappa)}$ consists of interval-valued *difference quotients* raised on the κth experimental data $\bar{\mathbb{X}}^{(\kappa)}$ and on step lengths $\bar{h}_\kappa := \bar{t}_{\kappa+1} - \bar{t}_\kappa$ between neighbouring samplings times [16, 20, 54]. As we make use of intervals we inserted *Chebychev* or *maximum norm* $\|\cdot\|_\infty$. When we turn to the *stability analysis* we can refer to the second class of parameters not comprised in the vector y and we can capitalize on the structure of $(\mathcal{CE})$ that allows a time-discretization represented by a sequence of matrix multiplications. The regions of stability can then be detected by the application of a combinatorial algorithm on polyhedra sequences [17].

6 Extended Dynamics of Regulation-Networks

The model $(\mathcal{CE})_{\text{target}}$ can be further enhanced when we additionally add a variable shift vector [43, 44, 45, 53, 65, 68]:

$$(\mathcal{ACE})_{\text{target}} \qquad \dot{X} \;=\; A(X)X + C(\mathbb{X}).$$

We call this decomposition a *normal form*, an *unfolding* [5, 9, 21, 25] or a *(generalized) additive model* [21, 47, 49, 50]. The affine linear shift term provides a more accurate data fitting and $C(\mathbb{X})$ represents environmental perturbations and contributions and may be, e.g., exponential, logarithmic, trigonometric or piecewise polynomial (splines). In addition, it displays special effects on each target variable emanated from any environmental item itself or cumulatively by all or several items working together or catalyzing each other. This cumulative effect might not be further divisible or quantifiable by the single effects.

We note that in $(\mathcal{ACE})_{\text{target}}$ we lost the multiplicative structure. This multiplicative form can be reconstructed as has been shown in [54, 65]. For this, the shift vector $C(\mathbb{X})$ of $(\mathcal{ACE})_{\text{gene}}$ has to be divided into the sum $\mathrm{W}(\mathbb{X})\check{\mathbb{X}} + \mathrm{V}(\mathbb{X})$ and we obtain the decomposition

$$(\mathcal{ACE}) \qquad \dot{X} \;=\; A(X)X + \mathrm{W}(\mathbb{X})\check{X} + \mathrm{V}(\mathbb{X}).$$

Here, the m-vector (of intervals) $\check{X}(t) = \big(\check{X}_1(t), \check{X}_2(t), \ldots, \check{X}_m(t)\big)^T$ comprises the levels of the m environmental factors that can affect the target variables and their variation. The *single effects* of the factors $\check{X}_\ell$ on the target data X_i can be incorporated by the weight matrix $\mathrm{W} = (\mathrm{w}_{i\ell})_{\substack{i=1,\ldots,n \\ \ell=1,\ldots,m}}$ into the system, and by this the n target items and the m environmental factors are individually matched. In addition, the column vector $\mathrm{V}(X) = (\mathrm{v}_i)_{i=1,\ldots,n}$ comprises all the cumulative effects of all (or several) environmental items influencing the target variables together. We note that the *total effect* of the environment on the value X_i is given by

$$\sum_{\ell=1}^{m} \mathrm{w}_{i\ell}(X)\check{X}_\ell \;+ \mathrm{v}_i.$$

We now define the *regulation matrix* $\check{A}(X) \;:=\; \big(\,\mathrm{W}(X)\,|\,\mathrm{diag}(\mathrm{V}(X))\,\big)$ of external effects, where the second block represents $\mathrm{V}(X)$ as a diagonal matrix with intervals on the diagonal. In addition, we set $\check{X}^\vee := \big(\check{X}^T, \mathrm{e}^T\big)^T$ with the n-vector $\mathrm{e} := (1, 1, \ldots, 1)^T$ and with $\mathrm{W}(X)\check{X} + \mathrm{V}(X) \;= \check{A}(X)\check{X}^\vee$ we obtain the following representation of $(\mathcal{ACE})$:

$$\dot{X} \;=\; A(X)X + \check{A}(X)\check{X}^\vee.$$

Finally, by introducing the $(d = m + 2n)$-vector $\mathbb{X} := \big(X, \check{X}^\vee\big)^T$, and the $(d \times d)$-matrix

$$\mathbb{A}(\mathbb{X}) = \begin{pmatrix} A(X) & \check{A}(X) \\ 0_{(m+n)\times n} & 0_{(m+n)\times(m+n)} \end{pmatrix} = \left(\begin{array}{c|cc} A(X) & \mathrm{W}(X) & \mathrm{diag}(\mathrm{V}(X)) \\ \hline 0_{m\times n} & 0_{m\times m} & 0_{m\times n} \\ 0_{n\times n} & 0_{n\times m} & 0_{n\times n} \end{array}\right),$$

we arrive at the extended (multiplicative) system $(\mathcal{CE})$ together with an extended initial value as follows:

$$(\mathcal{CE}) \qquad \dot{\mathbb{X}} = \mathbb{A}(\mathbb{X})\mathbb{X}, \qquad \mathbb{X}^{(0)} = \mathbb{X}(t_0) = \begin{pmatrix} X^{(0)} \\ \check{X}^{\vee,0} \end{pmatrix}.$$

We note that we have not included any environmental dynamics, but our modeling framework allows us to do this. In fact, by turning the 0 matrices in the second and the third (block) columns of $\mathbb{A}(\mathbb{X})$ to matrices which are different from 0, we can permit variable and interacting factors of the environment. Allowing also the 0 matrices in the first column to have nonzero entries, then this would express that the target variables influence various items of the environment (cf. Figure 1). In addition, the vector $\mathrm{V}(X)$ and the weight matrix $\mathrm{W}(X)$ could also depend on the variable $\check{X}$ or even $\check{X}^{\vee}$. This higher generality of $(\mathcal{CE})$ could also be implied into the parameter estimation from Section 9. We note that this generalization will become important for the introduction of the *eco-finance networks* in Section 13 and the related examples of CO_2-emissions control and portfolio optimization. For a stability analysis of the time-continuous model $(\mathcal{CE})$ we refer to [60, 61, 62].

T → T	E → T	CE → T
T → E	E → E	CT → E
$0_{n\times n}$	$0_{n\times m}$	$0_{n\times n}$

Figure 1: The regulation matrix. The first row describes the dynamics of the target items, depending on the target values (T), the single effects of the environmental items (E) and the cumulative environmental effects (CE). The second row describes the dynamics of the environmental items according to the single effects of the target variables (T), the states of the environmental items (E) and the cumulative effects of the target items (CT). The last row comes from the dimensional extension of the system that allows the representation in multiplication form.

7 The Time-Discretized Model

For a numerical analysis of our time-continuous modeling we can apply *Runge-Kutta methods* [13]. For example, when we use Heun's method on the system $(\mathcal{CE})$ we obtain the following time-discrete equation:

$$\begin{aligned}\mathbb{X}^{(k+1)} &= \mathbb{X}^{(k)} + \frac{h_k}{2}\mathbb{A}\big(\mathbb{X}^{(k)}\big)\mathbb{X}^{(k)} + \frac{h_k}{2}\mathbb{A}\big(\mathbb{X}^{(k)} + h_k\mathbb{A}\big(\mathbb{X}^{(k)}\big)\mathbb{X}^{(k)}\big)\cdot\Big(\mathbb{X}^{(k)} + h_k\mathbb{A}\big(\mathbb{X}^{(k)}\big)\mathbb{X}^{(k)}\Big)\\ &= \left[I + \frac{h_k}{2}\mathbb{A}\big(\mathbb{X}^{(k)}\big) + \frac{h_k}{2}\mathbb{A}\big(\mathbb{X}^{(k)} + h_k\mathbb{A}\big(\mathbb{X}^{(k)}\big)\mathbb{X}^{(k)}\big)\big(I + h_k\mathbb{A}\big(\mathbb{X}^{(k)}\big)\big)\right]\mathbb{X}^{(k)}\\ &= \mathbb{A}^{(k)}\mathbb{X}^{(k)} \quad (k \in \mathbb{N}_0).\end{aligned}$$

This equation allows a representation in "multiplication-form":

$$(\mathcal{DE}) \qquad \mathbb{X}^{(k+1)} = \mathbb{A}^{(k)}\mathbb{X}^{(k)}.$$

With this model we can calculate predictions of future values. For this we introduce the data vector $\bar{\mathbb{X}}^{(\kappa)} := \big((\bar{X}^{(\kappa)})^T, (\check{X}^{\vee,\kappa})^T\big)^T$ $(\kappa = 0, 1, \ldots, l-1)$, which comprises the results

from measurements of the target and the environmental items. The *predictions* are denoted by $\widehat{\mathbb{X}}^{(\kappa)}$ and we set $\widehat{\mathbb{X}}^{(0)} = \mathbb{X}^{(0)}$. The kth prediction is then calculated by

$$\widehat{\mathbb{X}}^{(k)} \ (:= \mathbb{X}^{(k)}) \ = \mathbb{A}^{(k-1)}(\mathbb{A}^{(k-2)} \cdots (\mathbb{A}^{(1)}(\mathbb{A}^{(0)}\mathbb{X}^{(0)})) \cdots) \ \ (k \in \mathbb{N}_0).$$

8 Extracting and Optimizing Regulation Networks

8.1 The Hybrid Model

Many financial, technical and biological systems exhibit switching behaviour. In the context of the regulatory networks under consideration we propose the following *hybrid model* [20, 54, 65]:

$$(\mathcal{HE}) \qquad \begin{array}{rcl} \dot{X}(t) & = & A_{s(t)}X(t) + \mathrm{W}_{s(t)}\check{X}(t) + \mathrm{V}_{s(t)}, \\ \text{where } s(t) & := & S(Q(X(t))) \text{ with} \\ Q(X(t)) & = & (Q_1(X(t)), Q_2(X(t)), \ldots, Q_n(X(t))), \quad \text{where} \\ Q_i(X(t)) & := & \begin{cases} 0, & X_i(t) < \theta_{i,1} \\ 1, & \theta_{i,1} \le X_i(t) < \theta_{i,2} \\ \vdots & \\ d_i, & \theta_{i,d_i} \le X_i(t) \ \ (i = 1, 2, \ldots, n). \end{cases} \end{array}$$

In $(\mathcal{HE})$ *thresholds of the target variables* are given by $\theta_{i,1} < \theta_{i,2} < \ldots < \theta_{i,d_i}$ and they can be defined by *Akaike's Information Criterion* [21] as in the original hybrid model presented in [20] and in the model extensions in [2, 19, 20, 27]. At these thresholds instantaneous changes of the parameter constellation can occur such that we have to choose a local model by the special selection of the $(n \times n)$-matrix $A_{s(t)}$, the $(n \times m)$-matrix $\mathrm{W}_{s(t)}$ and the n-vector $\mathrm{V}_{s(t)}$ (all three ones over intervals). The function $Q : \mathbb{R}^n \to \mathbb{N}_0^n$ implies the threshold constellation, and $S(Q(X))$ indicates where in the state space the system is placed at X, and which matrices and vectors A, W, V have to be chosen to specify the system such that the given data are approximated best. The function $S : \mathbb{N}_0^n \to \mathbb{N}_0$ must be injective, such that a different triplet (A,W,V) is used whenever a threshold is traversed. By this construction, the thresholds define a partition in subparallelpipes and the hybrid system $(\mathcal{HE})$ reduces in each subparallelpipe $\mathcal{P}^*$ to a system of ordinary linear differential equations that can be solved analytically. For this we have to extract the parametric unknowns $A_{s(t)}$, $\mathrm{W}_{s(t)}$ and $\mathrm{V}_{s(t)}$ from the given data. We note that we make use of binary and constant environmental data $\bar{\bar{X}}^{(\kappa)}$ $(\kappa = 0, 1, \ldots, l-1)$, but this data could also be variable in a more refined modeling.

8.2 Mixed-Integer Parameter Estimation

For an estimation of parameters we have to minimize the quadratic error between the difference quotients $\dot{\bar{X}}^{(\kappa_\alpha)}$ and the right-hand side of the differential equations evaluated at the finitely many measurement intervals $\bar{X}^{(\kappa_\alpha)} \in \mathcal{P}^*$ $(\alpha = 0, 1, \ldots, l^* - 1)$ which are lying in the regarded regime $\mathcal{P}^*$ takes the following form:

$$(\mathcal{HLS}) \qquad \min_{(a_{ij}^*),(\mathrm{W}_{i\ell}^*),(\mathrm{V}_i^*)} \sum_{\alpha=0}^{l^*-1} \left\| A^* \bar{X}^{(\kappa_\alpha)} + \mathrm{W}^* \bar{\bar{X}}^{(\kappa_\alpha)} + \mathrm{V}^* - \dot{\bar{X}}^{(\kappa_\alpha)} \right\|_\infty^2 .$$

In $(\mathcal{HLS})$, $\|\cdot\|_\infty$ stands for the *Chebychev norm* of the set inserted, i.e., it is the maximum norm with respect to the vector-valued functions defined by (independent) parametrization

which we get from the interval-valued entries of M^*, W^* and V^* as well as the ones of the vectors $\bar{X}^{(\kappa_\alpha)}$, $\bar{\bar{X}}^{(\kappa_\alpha)}$ and $\dot{\bar{X}}^{(\kappa_\alpha)}$, respectively. The classical "scalar" version of ($\mathcal{HLS}$), i.e., Gaussian approximation, can be canonically treated by building the partial derivatives with respect to the unknowns and equating them to 0. Then, one has to solve the resulting *normal equations*, which are linear in the unknown parameters a_{ij}^*, $\mathrm{w}_{i\ell}^*$ and v_i^*, e.g., by Gaussian elimination method algorithm. But ($\mathcal{HLS}$) is a generalized Chebychev approximation problem; since it can equivalently be written as a semi-infinite optimization problem (cf. [66]), we get access to the applicable methodology of SIP.

As nowadays high-throughput technologies are available, regulation networks are very large. Therefore, for practical reasons we have to rarefy them by diminishing the number of arcs [54, 65]. Here, upper bounds on the outdegrees of nodes (the variables) are introduced firstly; then, these constraints are further weakened by a continuous way of model improvement. We shortly recall this process in our interval-valued generalized Chebychevian way [63]. Firstly, we define the Boolean matrices and vectors, by $\chi = (\chi_{ij})_{i,j=1,\ldots,n}$, $\Xi = (\xi_{i\ell})_{\substack{i=1,\ldots,n\\ \ell=1,\ldots,m}}$, $Z = (\zeta_i)_{i=1,\ldots,n}$ with

$$\chi_{ij} := \begin{cases} 1, & \text{provided target item } j \text{ regulates target item } i \\ 0, & \text{if target item } j \text{ does } \textit{not} \text{ regulate target item } i, \end{cases}$$

$$\xi_{i\ell} := \begin{cases} 1, & \text{provided environmental item } \ell \text{ regulates target item } i \\ 0, & \text{if environmental item } \ell \text{ does } \textit{not} \text{ regulate target item } i, \end{cases}$$

$$\zeta_i := \begin{cases} 1, & \text{provided the environment cumulatively regulates target item } i \\ 0, & \text{if the environment does } \textit{not} \text{ cumulatively regulate target item } i. \end{cases}$$

The *outdegrees* $\sum_{i=1}^n \chi_{ij}$, $\sum_{i=1}^n \xi_{i\ell}$ and $\sum_{i=1}^n \zeta_i$ count the numbers of target items regulated by target item j, by environmental item ℓ or by the cumulative environment, respectively. Herewith, our parameter estimation task becomes a (generalized) *mixed-integer Chebychev approximation problem*

$$\min_{(a_{ij}^*),(\mathrm{W}_{i\ell}^*),(\mathrm{V}_i^*),(\chi_{ij}),(\xi_{i\ell}),(\zeta_i)} \sum_{\alpha=0}^{l^*-1} \left\| A^* \bar{X}^{(\kappa_\alpha)} + \mathrm{W}^* \bar{\bar{X}}^{(\kappa_\alpha)} + \mathrm{V}^* - \dot{\bar{X}}^{(\kappa_\alpha)} \right\|_\infty^2$$

$$(\mathcal{MICP}) \qquad \text{subject to} \begin{cases} \sum_{i=1}^n \chi_{ij} & \le & \alpha_j & (j = 1, 2, \ldots, n) \\ \sum_{i=1}^n \xi_{i\ell} & \le & \beta_\ell & (\ell = 1, 2, \ldots, m) \\ \sum_{i=1}^n \zeta_i & \le & \gamma & \\ a_{ii} & \ge & \delta_{i,\min} & (i = 1, 2, \ldots, n). \end{cases}$$

The connectivity of the network could be strongly restricted by the loss of the edges emanating at a few target items which are considered to play a very important role in regulation, i.e., to have very high outdegrees ("knockout"; [18]). This can be the result of perturbations caused by the environment and affecting the problem ($\mathcal{MICP}$) with its rigid (exclusive) binary constraints. We therefore replace them by continuous constraints in Section 9.

9 Improved Modeling by GSIP Extension

9.1 The GSIP Extension

The *mixed-integer Chebychev approximation problem* ($\mathcal{MICP}$) includes rigid binary constraints. To alleviate the effects of these constraints we replace the binary variables χ_{ij}, $\xi_{i\ell}$

and ζ_i by real variables $p_{ij}, q_{i\ell}, r_i \in [0,1]$ which linearly depend on the elements of a_{ij}, $\mathrm{w}_{i\ell}$ and v_i (also interpretable as probabilities) and assume some reasonable box constraints. By this, the values $\sum_{j=1}^{n} p_{ij}(a_{ij}^*)$, $\sum_{i=1}^{m} q_{i\ell}(\mathrm{w}_{i\ell}^*)$ and $\sum_{i=1}^{m} r_i(\mathrm{v}_i^*)$ have become interval-valued approximations of the numbers of target items regulated by target item j, environmental item ℓ and cumulative environment, respectively. All this leads us to a *continuous optimization problem* [54, 63, 65, 66]. Having solved the continuous optimization problem, we could return the binary variables and, hence, network rarefaction, by rounding or staying below some small prescribed values $\varepsilon_{ij}, \varepsilon_{i\ell}, \varepsilon_i \in [0,1)$, respectively [65].

The environment can seriously affect the connectedness between the target items. For those reasons, the papers [54, 65] implied all the possible convex combinations of the environmental effects into the inequalities about the bounded outdegrees. The *set of combined environmental effects* is defined as the convex hull of all the vectors $\mathrm{w}_{i\ell}^* e_{a(i-1)+\ell}$ and $\mathrm{v}_i^* e_{mn+i}$:

$$\begin{aligned} Y(\mathrm{V}^*,\mathrm{W}^*) \;:=\; & \mathrm{conv}\Big(\big\{ \mathrm{w}_{i\ell}^* e_{m(i-1)+\ell} \,\big|\, i=1,2,\ldots,n;\ \ell=1,2,\ldots,m \big\} \\ & \qquad \cup \big\{ \mathrm{v}_i^* \sigma_{i,m+1} e_{mn+i} \,\big|\, i=1,2,\ldots,n \big\} \Big) \\ =\; & \left\{ \sum_{\substack{i=1,\ldots,n,\\ \ell=1,\ldots,m}} \sigma_{i\ell} \mathrm{w}_{i\ell}^* e_{m(i-1)+\ell} + \sum_{i=1,\ldots,n} \sigma_{i,m+1} \mathrm{v}_i^* e_{mn+i} \;\middle|\; \right. \\ & \quad \sigma_{i\tau} \geq 0 \ (i=1,2,\ldots,n;\ \tau=1,2,\ldots,m+1), \\ & \quad \left. \sum_{\substack{i=1,\ldots,n\\ \tau=1,\ldots,m+1}} \sigma_{i\tau} = 1 \right\}, \end{aligned}$$

with e_η denoting the ηth $((m+1)n)$-dimensional unit vector $(0,\ldots,1,\ldots,0)^T$. Formally, we can write $Y(\mathrm{V}^*,\mathrm{W}^*)$ as a parallelpipe [61]

$$Y(\mathrm{V}^*,\mathrm{W}^*) = \prod_{\substack{i=1,\ldots,n\\ \ell=1,\ldots,m}} [0, \mathrm{w}_{i\ell}^*] \times \prod_{i=1,\ldots,n} [0, \mathrm{v}_i^*].$$

Now, we get our (generalized) *relaxed Chebychev approximation problem*:

$$(\mathcal{RCP}) \quad \min_{(a_{ij}^*),(\mathrm{W}_{i\ell}^*),(\mathrm{V}_i^*)} \sum_{\alpha=0}^{l^*-1} \left\| A^* \bar{X}^{(\kappa_\alpha)} + \mathrm{W}^* \bar{\bar{X}}^{(\kappa_\alpha)} + \mathrm{V}^* - \dot{\bar{X}}^{(\kappa_\alpha)} \right\|_\infty^2,$$

subject to

$$\begin{array}{rcccll} \sum_{i=1}^{n} p_{ij}(a_{ij}^*, y) & \leq & \alpha_j(y) & & & (y \in Y(\mathrm{V}^*,\mathrm{W}^*);\ j=1,2,\ldots,n), \\ \sum_{i=1}^{m} q_{i\ell}(\mathrm{w}_{i\ell}^*, y) & \leq & \beta_\ell(y) & & & (y \in Y(\mathrm{V}^*,\mathrm{W}^*);\ \ell=1,2,\ldots,m), \\ \sum_{i=1}^{m} r_i(\mathrm{v}_i^*, y) & \leq & \gamma(y) & & & (y \in Y(\mathrm{V}^*,\mathrm{W}^*)), \\ \delta_{i,\min} & \leq & a_{ii}^* & & & (i=1,2,\ldots,n), \\ \underline{a}_{ij}^* & \leq & a_{ij}^* & \leq & \overline{a}_{ij}^* & (i,j=1,2,\ldots,n), \\ \underline{\mathrm{w}}_{i\ell}^* & \leq & \mathrm{w}_{i\ell}^* & \leq & \overline{\mathrm{w}}_{i\ell}^* & (i=1,2,\ldots,n;\ \ell=1,2,\ldots,m), \\ \underline{\mathrm{v}}_i^* & \leq & \mathrm{v}_i^* & \leq & \overline{\mathrm{v}}_i^* & (i=1,2,\ldots,n). \end{array}$$

Now we compare $\underline{a}_{ii}^*$ and $\delta_{i,\min}$ and choose the largest of the two values as a single lower bound instead ($\delta_{i,\min} < \overline{a}_{ii}^*$ provided). As given in the objective function by generalized Chebychev approximation, this uniform interpretation of the "$\leq$" conditions amounts to the SIP character of $(\mathcal{RCP})$. By the additional coupling of our inequality constraint set

$Y(\mathrm{V}^*, \mathrm{W}^*)$ with the states $(\mathrm{V}^*, \mathrm{W}^*)$, $(\mathcal{RCP})$ even becomes a GSIP problem. In the objective function, the terms with the κth Chebychev norm $\|\cdot\|_\infty$ are nonsmooth max-type functions $(\kappa = 0, 1, \ldots, l^* - 1)$. By the following standard technique, $(\mathcal{RCP})$ becomes smoothly modeled. For each max-type function, we introduce a new coordinate τ_κ (in addition to the unknowns of $(\mathcal{RCP})$), considered as a new coordinate and as a uniform bound for the squared Euclidean norms of the elements inside the Chebychev norms. Herewith, we minimize the sum of the bounds. As new inequalities we just introduce these bounding conditions; we write them so that the Euclidean norms of all the elements inside the Chebychev norms have uniformly to stay below the corresponding bounds.

9.2 GSIP for Regulation Networks

When we apply GSIP for our regulatory network problem $(\mathcal{RCP})$ we obtain the general program form

$$\mathcal{P}_{\mathcal{GSI}}(f,h,g,u,v) \qquad \left\{ \begin{array}{l} \text{minimize } f(x) \text{ on } M_{\mathcal{GSI}}[h,g], \text{ where} \\ M_{\mathcal{GSI}}[h,g] := \big\{ x \in \mathbb{R}^d \,\big|\, h_i(x) = 0 \ (i \in I), \\ \qquad\qquad g^j(x,y) \geq 0 \ (y \in Y^j(x), \ j \in J) \big\}, \end{array} \right\} \quad (\mathcal{A}_1)$$

with $|I|, |J| < \infty$, and with sets $Y^j = Y^j(x)$ defined as *finitely constrained* $(\mathcal{F})$ feasible sets [59]. For each $x \in \mathbb{X}^d$, we have a representation

$$\left. \begin{array}{rcl} Y^j(x) & = & M_{\mathcal{F}}[u^j(x,\cdot), v^j(x,\cdot)] \\ & := & \big\{ \, y \in \mathbb{R}^q \,\big|\, u_k(x,y) = 0 \ (k \in K^j), \ v_\ell(x,y) \geq 0 \ (\ell \in L^j) \, \big\} \end{array} \right\} \quad (\mathcal{A}_2)$$

with finite sets K^j and L^j. The model $(\mathcal{A}_1)$-$(\mathcal{A}_2)$ allows equality constraints on both the upper (x-) level and lower (y-) level representing, e.g., further restrictions, reactions or balance equations [54, 63, 65]. The outdegree constraints in $(\mathcal{RCP})$ may be assumed to be of class C^2, too. The bounds guarantee that the feasible set $M_{\mathcal{GSI}}[h,g]$ is compact in the projective sense of the original $2(n^2 + mn + n)$ unknowns (with intervals encoded by tuples of endpoints), but not in the "height" dimensions of the new coordinates τ_κ. This noncompactness can be overcome as shown in [56, 59]. Here, the sets $Y^j(x)$ are compact and fulfill the *Linear Independence Constraint Qualification* (*LICQ*), an appropriate choice of the overall box constraints provided. The works [54, 59, 65, 66] provide more detailed discussions and generalizations of GSIP.

9.3 Structural Stability for Regulation Networks

In this subsection we state the main theorem on *structural stability* of our regulation networks. *Perturbations* of the form $(f,h,g,u,v) \mapsto (\tilde{f},\tilde{h},\tilde{g},\tilde{u},\tilde{v})$ may be caused, e.g., by *outliers of parallelpipes*, *"perturbed" problems and networks* and certain kinds of *errors, imprecision and uncertainty* [54, 65]. The strong Whitney topology C^2_S [24] serves as a "measure" of perturbations so that asymptotic aspects are taken into account. If the perturbed and the arbitrarily slightly unperturbed lower level sets of its objective function are homeomorphic to each other, under some correspondence between the levels, we call $(\mathcal{RCP})$ *structurally stable* [24, 26, 56, 59]. Now, we can carry over and state the *Characterization Theorem on Structural Stability for Regulation Networks* from [54, 65] for $(\mathcal{RCP})$ (for details cf. [57, 58, 59]). Our main theorem basically states that structural stability can just be *characterized* by two well-known regularity conditions and a more technical one:

Characterization Theorem on Structural Stability for Regulation Networks. [63, 66]
The optimization problem $\mathcal{P}_{\mathcal{GSI}}(f,h,g,u,v)$ on regulatory networks is structurally stable, if and only if the following triplet of conditions $\mathcal{C}_{1,2,3}$ is satisfied:

C_1. EMFCQ holds for $M_{\mathcal{GSI}}[h,g]$.

C_2. All the generalized-ordinary ($\mathcal{G}$-$\mathcal{O}$) Kuhn-Tucker points $\overline{x}$ of $\mathcal{P}_{\mathcal{GSI}}(f,h,g,u,v)$ are ($\mathcal{G}$-$\mathcal{O}$) strongly stable.

C_3. For each two different $\mathcal{G}$-$\mathcal{O}$ Kuhn-Tucker points $\overline{x}^1 \neq \overline{x}^2$ of $\mathcal{P}_{\mathcal{GSI}}(f,h,g,u,v)$ the corresponding critical values are different (separate), too: $f(\overline{x}^1) \neq f(\overline{x}^2)$.

This characterization theorem helps for a well understanding of the topological "landscape" of regulation networks, for their perturbational behaviour and for the development of numerical procedures. For example, we can consider "mountain paths" (saddle points) between any two candidate networks being given by local minimizers of ($\mathcal{RCP}$). All the points around candidate solutions can be regarded as potential networks which may be obtained after perturbations [57, 58, 59]. They may be outcomes of underlying constellations in the experimental design which may have to be reconstructed, which is an inverse problem. In terms of testing the *goodness of data fitting*, the lower level sets can be interpreted as confidence regions around the parameters estimated. The size of these regions is basically governed by the steepness of the function around the solution. In cases where a local or global minimizer is very steep, we can associate this with stability, whereas flatness is more likely related with instability [66]. For a better analytical understanding of ($\mathcal{RCP}$) and its solution, we identify possible pathologies in terms of one or more of the conditions $\mathcal{C}_{1,2,3}$ violated.

We point out a relation to *conic programming* (CP), however, in a GSIP sense. If in ($\mathcal{RCP}$) all the functions defining the constraints are linear and the squares on the Chebychev norms deleted, then we obtain such a CP problem. If we square both the linear constraint functions and the bounds, we arrive at the special case of CP called *conic quadratic programming* (*CQP*) [49]. In CP problems, *interior point methods* can be introduced and efficiently applied.

10 On the Numerics of the Linear Inverse Problem

Our parameter estimation problems, as far as they are linear, do not directly have the canonical form of linear least-squares (or inverse) problems. Indeed, the unknowns are matrices here rather than vectors. However, our problem can be represented in a canonical way such that the coefficient matrix reveals a block-diagonal form [16]. In case of sufficiently many blocks and zeros in them, the matrix is *sparse*. Already in the underlying problem form $(\mathcal{CE})_{ext}$, there are many vanishing entries. *Kazcmarz algorithm* with its different versions of iterative projection methods [6] is an important and advisable way for approximately solving linear inverse (or feasibility) problems with a sparse coefficient matrix. Numerically, it is important to have or otherwise to prepare neighbouring linear conditions (defining hyperplanes) to be as "distant" as possible. The work [8] can be regarded as a generalization of this idea to other types of feasibility and optimization problems; there are convex sets instead of hyperplanes. In [8], a new version of the *successive projection algorithms* introduced by Brègman and von Neumann [7, 55] is given. These algorithms are widely applicable in medical imaging, computerized tomography and signal processing. The authors study the convergence and propose a finite termination criterion allowing to analyze the complexity.

11 Modeling by Stochastic Differential Equations

A further interesting approach to our modeling, in particular in financial sciences, is based on *stochastic differential equations* (SDE). Such an equation is typically given by

$$\begin{aligned}\dot{X}(t) &= a(X,t) + b(X,t)\delta_t \quad (t \in [0,\infty)),\\ X(0) &= x_0,\end{aligned}$$

where a is the deterministic part, $b\delta_t$ is the stochastic part, and δ_t denotes a generalized stochastic process [28, 62]. An example for a generalized stochastic process is white noise. Suppose that W_t is a generalized version of a Wiener process, i.e., a time-continuous process with the property $W_t \sim N(0,t)$ $(0 \le t \le T)$. To obtain our approximate and a smoothed model, we treat W_t as differentiable. Then, white noise δ_t is defined as $\delta_t = \dot{W}_t = dW_t/dt$ and a Wiener process can be obtained by smoothing the white noise. If we replace $\delta_t dt$ by dW_t in our SDE, we obtain

$$dX_t = a(X_t,t)dt + b(X_t,t)dW_t,$$

where $a(X_t,t)$ and $b(X_t,t)$ are drift and diffusion terms, respectively, and X_t is a solution which we try to find based on the experimental data. Since we do not know the distribution of X_t, we want to simulate its values. For this reason, we simulate a discretized version of SDE. We consider the *Milstein scheme* and obtain

$$\begin{aligned}X_{k+1} = X_k &+ a(X_k,t)(t_{k+1}-t_k) + b(X_k,t)(W_{k+1}-W_k)\\ &+ \frac{1}{2}(b'b)(X_j,t)\Big(\big(W_{k+1}-W_k\big)^2 - \big(t_{k+1}-t_k\big)\Big)\end{aligned}$$

as an approximation for X_t (here, we understand X_k in the sense of our estimation $\widehat{X}^{(k)}$ and the prime "$'$" denotes the derivative with respect to t). When we refer to the finitely many sample points $\big(\overline{X}_j, \bar{t}_j\big)$, we get the discrete approximation

$$\dot{\overline{X}}_\kappa = a\big(\overline{X}_\kappa, \bar{t}_\kappa\big) + b\big(\overline{X}_\kappa, \bar{t}_\kappa\big)\,\frac{\Delta W_\kappa}{\bar{h}_\kappa} + \frac{1}{2}(b'b)\big(\overline{X}_\kappa, \bar{t}_\kappa\big)\left(\frac{(\Delta W_\kappa)^2}{\bar{h}_\kappa} - 1\right)$$

for $\kappa = 0, 1, \ldots, N$. Here, the vector $\dot{\overline{X}}_\kappa$ represents difference quotients based on the κth experimental data and on step lengths $\bar{h}_\kappa := \bar{t}_{\kappa+1} - \bar{t}_\kappa = \Delta\bar{t}_\kappa$ between neighbouring sampling times. This relation cannot hold in an exact sense since we consider real data, but it is satisfied best in the *approximate* sense of least squares of errors. The increments ΔW_t are independent on non-overlapping intervals and we have $\mathrm{Var}\big(\Delta\overline{W}_t\big) = \Delta\bar{t}_\kappa$. Hence, the increments having a normal distribution can be simulated by normal distributed random numbers $\overline{Z}_\kappa$ and we obtain a discrete model:

$$\Delta\overline{W}_t = \overline{Z}_\kappa\sqrt{\Delta\bar{t}_\kappa},\ \overline{Z}_\kappa \sim N(0,1).$$

If we use this in our discretized equation, we obtain

$$\dot{\overline{X}}_\kappa = a\big(\overline{X}_\kappa, \bar{t}_\kappa\big) + b\big(\overline{X}_\kappa, \bar{t}_\kappa\big)\,\frac{\overline{Z}_\kappa}{\sqrt{\bar{h}_\kappa}} + \frac{1}{2}(b'b)\big(\overline{X}_\kappa, \bar{t}_\kappa\big)\big(\overline{Z}_\kappa^2 - 1\big).$$

We can rewrite this as

$$\dot{\overline{X}}_\kappa = \overline{G}_\kappa + \overline{H}_\kappa\bar{c}_\kappa + \big(\overline{H}'_\kappa\overline{H}_\kappa\big)\,\bar{d}_\kappa,$$

where

$$\bar{c}_\kappa := \frac{\overline{Z}_\kappa}{\sqrt{\bar{h}_\kappa}},\ \bar{d}_\kappa := \frac{1}{2}\big(\overline{Z}_\kappa^2 - 1\big),\ \overline{G}_\kappa := a\big(\overline{X}_\kappa, \bar{t}_\kappa\big),\ \overline{H}_\kappa := b\big(\overline{X}_\kappa, \bar{t}_\kappa\big).$$

The unknowns $\overline{G}_\kappa$ and $\overline{H}_\kappa$ can be determined by the optimization problem

$$\min_y \ \sum_{\kappa=1}^{l-1} \left(\dot{\overline{X}}_\kappa - \big(\overline{G}_\kappa + \overline{H}_\kappa \bar{c} + \big(\overline{H}'_\kappa \overline{H}_\kappa\big)\,\bar{d}\big) \right)^2,$$

where the vector y comprises all the parameters in the Milstein model. As the data may have a high variation we must use a parameter estimation method which will give a smoother approximation to the data. In [46, 48] *splines* were used to avoid large oscillations observed for high degree polynomial approximation. In addition, a *penalized residual sum of squares* for SDE and a related *Tikhonov regularization problem* (that could be solved with MATLAB Regularization Toolbox) have been proposed. Alternatively to the concept of Tikhonov regularization we can apply *conic quadratic programming* and we refer to [23, 46, 48] for further details and to [23] for a study on the prediction of the *credit-default risk* that already demonstrated the value of generalized additive models.

12 On Spline Regression Applied in an Additive Model

In [63, 66], spline regression has firstly become introduced into our modeling and analysis. This approach has been generalized to the interval-valued case [61]. There, we understand integrals with interval-valued integration endpoints as families of integrals. *Splines*, i.e., smooth piecewise polynomial functions [12], are very suitable to approximate observed data $\bar{\mathbb{X}}$ without any significant asymptotic growths $\to \pm\infty$. They are described as linear combinations of basis splines and approximate the data $(\bar{t}_\kappa, \dot{\bar{X}}^{(\kappa)})$. In $(\mathcal{ACE})$, we use splines $f_\alpha(X_\alpha)$ per entry of $A(X)$, $\mathrm{W}(X)$ and $\mathrm{V}(X)$, within an approach which we call *separation of variables*; i.e., with base (B-) splines $h^{1,i,j}_{\alpha,\gamma}(X_\alpha)$, $h^{2,i,j}_{\alpha,\gamma}(X_\alpha)$, $h^{3,i,j}_{\alpha,\gamma}(X_\alpha)$, evaluated at the expression levels of the αth target variable, and partial intercepts $\beta_0^{1,i,j}$, $\beta_0^{2,i,j}$, $\beta_0^{3,i,j}$, depending on $\dot{X}^{(\kappa)}$ $(\kappa = 0, 1, \ldots, l-1)$ [63, 66]. We obtain the representation

$$a_{ij}(X) = \beta_0^{1,i,j} + \sum_{\alpha=1}^{n} f_\alpha^{1,i,j}(X_\alpha) = \beta_0^{1,i,j} + \sum_{\alpha=1}^{n} \sum_{\gamma=1}^{p_{ij}} \theta^{1,i,j}_{\alpha,\gamma} h^{1,i,j}_{\alpha,\gamma}(X_\alpha) \quad (i,j = 1,2,\ldots,n)$$

and

$$\mathrm{w}_{i\ell}(X) = \beta_0^{2,i,\ell} + \sum_{\alpha=1}^{n} f_\alpha^{2,i,\ell}(X_\alpha) = \beta_0^{2,i,\ell} + \sum_{\alpha=1}^{n} \sum_{\varphi=1}^{q_{i\ell}} \theta^{2,i,\ell}_{\alpha,\varphi} h^{2,i,\ell}_{\alpha,\varphi}(X_\alpha)$$

as well as

$$\mathrm{v}_i(X) = \beta_0^{3,i} + \sum_{\alpha=1}^{n} f_\alpha^{3,i}(X_\alpha) = \beta_0^{3,i} + \sum_{\alpha=1}^{n} \sum_{\nu=1}^{r_i} \theta^{3,i}_{\alpha,\nu} h^{3,i}_{\alpha,\nu}(X_\alpha)$$

with $i = 1, \ldots, n;\ l = 1, \ldots, m$. A great benefit of using the base splines is provided by the following recursion, where we denote the kth order base spline by $h_{\eta,k}$ (a polynomial of degree $k-1$) with knots x_η:

$$h_{\eta,1}(x) = \begin{cases} 1 & \text{, if } x_\eta \le x < x_{\eta+1} \\ 0 & \text{, otherwise,} \end{cases}$$

$$h_{\eta,k}(x) = \frac{x - x_\eta}{x_{\eta+k} - x_\eta}\, h_{\eta,k-1}(x) + \frac{x_{\eta+k+1} - x}{x_{\eta+k+1} - x_{\eta+1}}\, h_{\eta+1,k-1}(x)$$

for all orders $k \geq 1$. In the above representation, $h^{1,i,j}_{\alpha,\gamma}(X_\alpha)$ are base splines evaluated at the expression levels of the αth target item. By the parameters $\beta_0^{1,i,j}$ we denote partial intercepts depending of the output data $\dot{X}^{(\kappa)}$ ($\kappa = 0, 1, \ldots, l-1$) (percentages of their averaged data). By this an additive separation of the variables is realized. However, this linear kind of interaction is not always given but can be considered as an approximation. Instead, below, we will come to a different interpretation of our *additive* functional structure by a clustering of the input data. This additivity may be regarded as a model richness which is intermediate in-between both affine linearity and a nonlinearity that takes into account more complex interactions and correlations between the variables or data clusters, respectively. Firstly, we choose splines degrees individually for each entry $a_{ij}(X)$. Likewise, we represent the entries of $\mathrm{W}(X)$ and $\mathrm{V}(X)$ by splines. Indeed, when using spline functions for the entries $\mathrm{w}_{i\ell}(X)$ and $\mathrm{v}_i(X)$ we must be careful since they are environmental effects influencing the target levels and their approximation. Since we consider these effects to be very small, they have a restricted effect represented by the selected spline degrees for $\mathrm{w}_{i\ell}(X)$ and $\mathrm{v}_i(X)$ not larger than those of $a_{ij}(X)$. Otherwise, the approximated levels of the target variables can become affected and this may imply instability in the parameter estimation [49]. To quantify that possible instability, we refer to the second order derivatives (curvature) of the model functions. Then, looking at the equation $(\mathcal{ACE})_{\mathrm{gene}}$, our model becomes fitted by minimizing the criterion of *penalized sum of squares* [21]:

$$\begin{aligned}
\mathrm{PRSS}(A, \mathrm{W}, \mathrm{V}) &= \sum_{\kappa=0}^{l-1} \left\| \dot{\bar{X}}^{(\kappa)} - A(\bar{X}^{(\kappa)})\bar{X}^{(\kappa)} - \mathrm{W}(\bar{X}^{(\kappa)})\bar{\breve{X}}^{(\kappa)} - \mathrm{V}(\bar{X}^{(\kappa)}) \right\|_\infty^2 \\
&\quad + \text{Penalty Term} \\
&= \sum_{\kappa=0}^{l-1} \sum_{i=1}^{n} \left(\dot{\bar{X}}_i^{(\kappa)} - \sum_{j=1}^{n} a_{ij}(\bar{X}^{\kappa})\bar{X}_j^{(\kappa)} - \sum_{\ell=1}^{m} \mathrm{w}_{i\ell}(\bar{X}^{(\kappa)})\bar{\breve{X}}_\ell^{(\kappa)} - \mathrm{v}_i(\bar{X}^{(\kappa)}) \right)^2 \\
&\quad + \text{Penalty Term}.
\end{aligned}$$

Here, $\|\cdot\|_\infty$ denotes the Chebychev norm. If we use our additive model approximations for $a_{ij}(X)$, $\mathrm{w}_{i\ell}(X)$ and $\mathrm{v}_i(X)$, then PRSS has the following form, where $(\cdot)''_{X_\alpha}$ denotes differentiation with respect to X_α:

$$\begin{aligned}
\text{Penalty Term} &= \sum_{i=1}^{n}\sum_{j=1}^{n} \left[\sum_{\alpha=1}^{n} \lambda_\alpha^{1,i,j} \left\| \int_{X_\alpha^L}^{X_\alpha^U} \left(f_\alpha^{1,i,j}(X_\alpha) X_j \right)''^2_{X_\alpha} \, dX_\alpha \right\|_\infty^2 \right] \\
&\quad + \sum_{i=1}^{n}\sum_{l=1}^{m} \left[\sum_{\alpha=1}^{n} \mu_\alpha^{2,i,\ell} \left\| \int_{X_\alpha^L}^{X_\alpha^U} \left(f_\alpha^{2,i,l}(X_\alpha) \breve{X}_l \right)''^2_{X_\alpha} \, dX_\alpha \right\|_\infty^2 \right] \\
&\quad + \sum_{i=1}^{n} \left[\sum_{\alpha=1}^{n} \varsigma_\alpha^{3,i} \left\| \int_{X_\alpha^L}^{X_\alpha^U} \left(f_\alpha^{3,i}(X_\alpha) \right)''^2_{X_\alpha} \, dX_\alpha \right\|_\infty^2 \right],
\end{aligned}$$

where $\lambda_\alpha^{1,i,j}$, $\mu_\alpha^{2,i,\ell}$, $\varsigma_\alpha^{3,i} \geq 0$ are penalty parameters, and X_α^L, X_α^U are lower and upper bounds of X_α. Here, $\breve{X}_l$ are the constant environmental factors and not depending on the levels of the target variable X_α; we may uniformly replace them by the averaged data

$\breve{X}_\ell := \frac{1}{l}\sum_{\kappa=0}^{l-1} \bar{\breve{X}}_l^{(\kappa)}$. Then, denoting $\phi_\alpha^{2,i,\ell} := \mu_\alpha^{2,i,\ell}\breve{X}_\ell^2$, the penalty term can be written as

$$\begin{aligned}\text{Penalty Term} = &\sum_{i=1}^{n}\sum_{j=1}^{n}\left[\sum_{\alpha=1}^{n}\lambda_\alpha^{1,i,j}\left\|\int_{X_\alpha^L}^{X_\alpha^U}\left(f_\alpha^{1,i,j}(X_\alpha)X_j\right)_{X_\alpha}^{''2}\,dX_\alpha\right\|_\infty^2\right]\\ &+\sum_{i=1}^{n}\sum_{\ell=1}^{m}\sum_{\alpha=1}^{n}\left[\phi_\alpha^{2,i,\ell}\left\|\int_{X_\alpha^L}^{X_\alpha^U}\left(f_\alpha^{2,i,\ell}(X_\alpha)\right)_{X_\alpha}^{''2}\,dX_\alpha\right\|_\infty^2\right]\\ &+\sum_{i=1}^{n}\left[\sum_{\alpha=1}^{n}\varsigma_\alpha^{3,i}\left\|\int_{X_\alpha^L}^{X_\alpha^U}\left(f_\alpha^{3,i}(X_\alpha)\right)_{X_\alpha}^{''2}\,dX_\alpha\right\|_\infty^2\right].\end{aligned}$$

Inside the integrals of the first sum terms, we find the squared second order derivatives to have the values $((X_j+\delta_{\alpha j})(f_\alpha^{1,i,j}(X_\alpha)X_j)_{X_\alpha}^{''}+\delta_{\alpha j}(f_\alpha^{1,i,j}(X_\alpha)X_j)_{X_\alpha}^{'})$, with Kronecker's delta symbol $\delta_{\alpha j}$ representing some "on/off" kind of activation/deactivation, such there is a shift in terms of first-order derivatives (denoted by $(\cdot)'_{X_\alpha}$), and a mixing effect by squaring. Using spline functions inside PRSS, putting

$$\begin{aligned}G(M,\mathrm{W},\mathrm{V}) &:= \sum_{\kappa=0}^{l-1}\sum_{i=1}^{n}\left(\dot{\bar{X}}_i^{(\kappa)} - \sum_{j=1}^{n}a_{ij}(\bar{X}^{(\kappa)})\bar{X}_j^{(\kappa)} - \sum_{l=1}^{m}\mathrm{w}_{il}(\bar{X}^{(\kappa)})\bar{\breve{X}}_l^{(\kappa)} - \mathrm{v}_i(\bar{X}^{(\kappa)})\right)^2\\ &=: \left\|U(\theta^1,\theta^2,\theta^3)\right\|_\infty^2\end{aligned}$$

and using the discretized form [49] for all members in the integral terms, then we can write each of them as $\left\|V_{i,\alpha,j}(\theta^1)\right\|_\infty^2$, $\left\|W_{i,\alpha,\ell}(\theta^2)\right\|_\infty^2$ and $\left\|Z_{i,\alpha}(\theta^3)\right\|_\infty^2$. Now, turning to a constrained rather than a penalized program, PRSS can be interpreted as an optimization problem of the following form:

$$\min_{t,\theta^1,\theta^2,\theta^3}\quad t,$$

where

$$\begin{aligned}\left\|U(\theta^1,\theta^2,\theta^3)\right\|_\infty^2 &\le t^2\\ \left\|V_{i,\alpha,j}(\theta^1)\right\|_\infty^2 &\le \mathrm{A}_{i,\alpha,j} \qquad (i,\alpha,j=1,2,\ldots,n)\\ \left\|W_{i,\alpha,\ell}(\theta^2)\right\|_\infty^2 &\le \mathrm{N}_{i,\alpha,\ell} \qquad (i,\alpha=1,2,\ldots,n;\ \ell=1,2,\ldots,m)\\ \left\|Z_{i,\alpha}(\theta^3)\right\|_\infty^2 &\le \mathrm{R}_{i,\alpha} \qquad (i,\alpha=1,2,\ldots,n)\\ t &\ge 0.\end{aligned}$$

This optimization problem has the form of a *conic quadratic programming* (*CQP*) problem, which can be solved by *interior points method* (*IPM*) [33, 34, 35, 49]. Except for very large-scale problems with dense matrices, these problems have a moderate complexity. As learned in [49], CQP and IPM are much more convenient than penalty methods connected with backfitting algorithm [21]. Conic programming is also helpful in clustering theory, especially, in computational biology [3, 4]. We note that among the basic kinds and important kinds of spline regression, MARS (multivariate adaptive repression spline) belongs, which uses natural, elementary base functions which are nonsmooth [15, 21]. The most widespread MARS algorithm bases on a forward step of setting up the model and minimizing the lack of fit, an a backward step on controlling the complexity by generalized cross-validation. In [51], an alternative to the backward step was proposed with the help conic quadratic programming [34], and Tikhonov regularization [6] which can be regarded as a penalization

techniques or multiobjective optimization for inverse problems. By the study [67] it has been demonstrated that this new approach coming from continuous optimization is very much competitive and even superior to the classical MARS, applied to different data sets.

13 Eco-Finance Networks

The models and analysis of the previous sections provide a conceptual framework for various problems in Operational Research. We illustrate this with an important example in the field of CO_2-emissions-control and an example of operational planning and portfolio optimization in the context of natural gas transportation systems. By this, our regulatory-networks are extended to the so-called *eco-finance networks*.

The model under consideration is the so-called *Technology-Emissions-Means Model* (in short: *TEM model*), developed by *S. Pickl* for the mathematical analysis of international collaborations and joint implementation programs (JI) in the framework of the Kyoto Protocol [36]. The TEM model integrates the simulation of the technical and financial parameters and describes the economical interactions between several actors (countries, companies) which intend to minimize their emissions by means of cooperative game theory. The players are linked by technical cooperations and the market, which expresses itself in the nonlinear time discrete dynamics of the TEM model [30, 37, 38, 39]. We denote by E_i the emissions caused by technologies T_i using financial means E_i, where the index i stands for the ith player ($i = 1, 2, \ldots, N$). The relationship between financial means and reduced emission in a JI program is given by

$$\Delta \mathsf{E}_i(k) = \sum_{j=1}^{N} \mathsf{em}_{ij}(k)\mathsf{M}_j(k),$$
$$\Delta \mathsf{M}_i(k) = -\lambda_i \mathsf{M}_i(k)(\overline{\mathsf{M}}_i - \mathsf{M}_i(k))(\mathsf{E}_i(k) + \varphi_i \Delta \mathsf{E}_i(k))$$

with

$$\Delta \mathsf{E}_i(k) := \mathsf{E}_i(k+1) - \mathsf{E}_i(k) \quad \text{and} \quad \Delta \mathsf{M}_i(k) := \mathsf{M}_i(k+1) - \mathsf{M}_i(k),$$

where the discrete times t_k are renamed by k. Furthermore, $\overline{\mathsf{M}}_i$ stands for the upper bounds for the financial investigations. The first equation describes the time-dependent behaviour of the emissions reduced so far by each player. These levels E_i are influenced by financial investigations M_j which are restricted by the second equation. We understand E_i as the reduced emissions of actor i in % and M_i as the financial means of actor i. The parameters φ_i are called *memory parameters*. Thus, the multiplication of $\Delta \mathsf{E}_i$ with φ_i can be regarded as a *memory effect*; this expression stands for the influence of earlier investments. The first part of the second equation resembles a logistic difference equation, where the proportional factor λ_i can be seen as a *growth parameter*. Each coefficient em_{ij} describes the effect on the emissions of the ith actor if the jth actor invests one unit of money for his technologies, e.g., devices of filters in energy production of consumption. This also shows how effective technology cooperations are, what is the kernel of the JI program. The parameters em_{ij} have to be determined empirically. The numerical examinations which show that chaotic behaviour can occur, underline the necessity of a control theoretic approach which is implied

by an additional control term in the second equation of the TEM model:

$$\mathsf{E}_i(k+1) = \mathsf{E}_i(k) + \sum_{j=1}^{N} \mathsf{em}_{ij}(k)\mathsf{M}_j(k),$$
$$\mathsf{M}_i(k+1) = \mathsf{M}_i(k) - \lambda_i \mathsf{M}_i(k)(\overline{\mathsf{M}}_i - \mathsf{M}_i(k))\left(\mathsf{E}_i(k) + \varphi_i \Delta \mathsf{E}_i(k)\right) + u_i(k).$$

We note that the TEM model relies on exact data, but this approach aims to model real-world processes, imprecisions and errors have to be considered. For this, in [60] an interval-valued reformulation within the framework of our regulation networks has been proposed and the TEM model has been structured as follows:

$$\left(\mathsf{E}^T, \mathsf{M}^T\right)^{T\,(k+1)} = M^{(k)}\left(\left(\mathsf{E}^T, \mathsf{M}^T\right)^{T\,(k)}\right)\left(\mathsf{E}^T, \mathsf{M}^T\right)^{T\,(k)}.$$

Having added the control parameter, we obtain the time-discrete dynamics

$$\begin{pmatrix} \mathsf{E} \\ \mathsf{M} \end{pmatrix}^{(k+1)} = M^{(k)}\left(\begin{pmatrix} \mathsf{E} \\ \mathsf{M} \end{pmatrix}^{(k)}\right)\begin{pmatrix} \mathsf{E} \\ \mathsf{M} \end{pmatrix}^{(k)} + \begin{pmatrix} 0 \\ u^{(k)} \end{pmatrix},$$

which we can represented by

$$(\mathcal{DE}) \qquad \mathbb{X}^{(k+1)} = \mathbb{A}^{(k)}\mathbb{X}^{(k)}.$$

Here, the matrices $\mathbb{A}^{(k)}$ incorporate the control variables. In this extended space notation, the variable $\mathbb{X}$ and entire dynamics $(\mathcal{DE})$ could be enriched by further environmental and, in particular, target items and relations. The shift vector $(0^T, (u^{(k)})^T)^T$ can be regarded as parametric and as a realization of $\mathrm{V}(X, \check{X}^\vee)$; then, our stability theory could be employed. According to how those matrices are adjusted, we arrive at different behaviours of stability or instability of $(\mathcal{DE})$ or of parameter estimation. As a dual alternative to that feedback-like realization by the vector $\mathrm{V}(X, \check{X}^\vee)$ which becomes incorporated into the matrix $\mathbb{A}^{(k)}$, the control vectors $u^{(k)}$ could also become integrated into $\mathbb{X}^{(k)}$. The time-dependent parameters $\mathsf{em}_{ij}^{(k)}$ can be treated in similar ways as the controls.

Finally, as a further application of our eco-finance networks we mention the *operational planning* for the "natural gas value chain", where the production (gas transportation and storage, processing) as well as the market situation (financial market, spot market, contract market) have to be considered. In [52] a portfolio optimization model for gas transport systems with the aim of production and market optimization has been proposed. For the arrangement of short term production plans, for market balancing (mixing physical production, spot trades) and for transportation booking and storage utilization - which could be interpreted as the economic key variables - various positions and resources on different time-scales with inherent uncertainty have to be considered. In particular, strategic plans (field and pipeline investments, long term contracts, production profiles, lifting agreements) and tactical plans (production plans, transportation plans, storage profiles) have to be observed, that built the environmental items in our eco-finance networks.

14 Conclusion

In the previous sections we have presented various models for the mathematical analysis of highly-interconnected systems under uncertainty. We have analyzed the dynamic interactions between a class of target variables and certain environmental items and explored

the structure of the underlying regulatory network. In addition, we conducted a parameter estimation and a stability analysis for the resulting models. Finally, we have shown that our modelling can be successfully applied to important problems from finance and technology and we have introduced the *eco-finance networks*.

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References

[1] M.U. Akhmet, J. Gebert, M. Lätsch, S.W. Pickl, G.-W. Weber and R. Wünschiers, Algorithmic computational biology: stability analysis of gene-expression patterns, *Journal of Computational Technologies* 9 (2004).

[2] M.U. Akhmet, J. Gebert, H. Öktem, S.W. Pickl and G.-W. Weber, An improved algorithm for analytical modeling and anticipation of gene expression patterns, *Journal of Computational Technologies* 10 (2005) 3–20.

[3] B. Akteke-Öztürk and G.-W. Weber, A survey and results on semidefinite and nonsmooth optimization for minimum sum of squared distances problem, Middle East Technical University, Institute of Applied Mathematics, Preprint 65 (2006).

[4] B. Akteke-Öztürk, G.-W. Weber and E. Kropat, Continuous optimization approaches for clustering via minimum sum of squares, in *The 20th International Conference, EURO Mini Conference " Continuous Optimization and Knowledge-Based Technologies " (EurOPT-2008)*, L. Sakalauskas, G.-W. Weber and E. K. Zavadskas (eds.), Vilnius Gediminas Technical University Publishing House " Technika ", 2008, pp. 253–258.

[5] H. Amann, *Gewöhnliche Differentialgleichungen*, Walter de Gruyter, Berlin, New York, 1983.

[6] A. Aster, B. Borchers and C. Thurber, *Parameter estimation and inverse problems*, Academic Press, Amsterdam, 2004.

[7] L.M. Brègman, The method of successive projection for finding a common point of convex sets, *Soviet. Math. Dokl.* 6 (1965) 688–692.

[8] W. Briec and B. Solonandrasana, Some remarks on a successive projection sequence, preprint, University of Perpignan (2006).

[9] T. Bröcker and L. Lander, *Differentiable Germs and Catastrophes*, London Mathematical Society Lecture Note Series 17, Cambridge University Press, London, 1975.

[10] T. Chen, H.L. He and G.M. Church, Modeling gene expression with differential equations, *Proc. Pacific Symposium on Biocomputing* (1999) 29–40.

[11] W.D. Collins and C. Hu, Fuzzily determined interval matrix games, `http://www-bisc.cs.berkeley.edu/BISCSE2005/Abstracts_Proceeding/Friday/FM3/Chenyi_Hu.pdf`

[12] D.M. Dubois and E. Kalisz, Precision and stability of Euler, Runga-Kutta and incursive algorithm for the harmonic oscillator, *International Journal of Computing Anticipatory Systems* 14 (2004) 21–36.

[13] T. Ergenç and G.-W. Weber, Modeling and prediction of gene-expression patterns reconsidered with Runge-Kutta discretization, *Journal of Computational Technologies* 9 (2004) 40–48.

[14] M. Fiedler, J. Nedoma, J. Ramik, J. Rohn and K. Zimmermann, *Linear optimization problems with inexact data*, Springer Verlag, Berlin, 2006.

[15] J.H. Friedman, Multivariate Adaptive Regression Splines, *The Annals of Statistics* 19 (1991) 1–67.

[16] J. Gebert, M. Lätsch, S.W. Pickl, N. Radde, G.-W. Weber and R. Wünschiers, Genetic networks and anticipation of gene expression patterns, *AIP Conference Proceedings* 718 (2004) 474–485.

[17] J. Gebert, M. Lätsch, S.W. Pickl, G.-W. Weber and R. Wünschiers, An algorithm to analyze stability of gene-expression pattern, *Discrete Applied Mathematics* 154 (2006) 1140–1156.

[18] J. Gebert, M. Lätsch, E.M.P. Quek and G.-W. Weber, Analyzing and optimizing genetic network structure via path-finding, *Journal of Computational Technologies* 9 (2004) 3–12.

[19] J. Gebert, H. Öktem, S.W. Pickl, N. Radde, G.-W. Weber and F.B. Yılmaz, Inference of gene expression patterns by using a hybrid system formulation – an algorithmic approach to local state transition matrices, in *Anticipative and predictive models in systems science I*, G.E. Lasker and D.M. Dubois (eds.), IIAS. Windsor, Ontario, 2004, pp. 63–66.

[20] J. Gebert, N. Radde and G.-W. Weber, Modelling gene regulatory networks with piecewise linear differential equations, *European J. Oper. Res.* 181 (2006) 1148–1165.

[21] T. Hastie, R. Tibshirani and J.H. Friedman, *The Elements of Statistical Learning – Data Mining, Inference and Prediction*, Springer, New York, 2001.

[22] M.D. Hoon, S. Imoto, K. Kobayashi, N. Ogasawara and S. Miyano, Inferring gene regulatory networks from time-ordered gene expression data of Bacillus subtilis using differential equations, *Pac. Symp. Biocomput.* (2003) 17–28.

[23] A. Işcanoğlu, G.-W. Weber and P. Taylan, Predicting Default Probabilities with Generalized Additive Models for Emerging Markets, invited Lecture, Graduate Summer School on New Advances in Statistics, METU, August 11-24, 2007, http://144.122.137.55/gweber/.

[24] H.T. Jongen, P. Jonker and F. Twilt, *Nonlinear Optimization in Finite Dimensions – Morse Theory, Chebyshev Approximation, Transversality, Flows, Parametric Aspects*, Kluwer Academic Publishers, Boston, 2000.

[25] H.T. Jongen and G.-W. Weber, On parametric nonlinear programming, *Ann. Oper. Res.* 27 (1990) 253–284.

[26] H.T. Jongen and G.-W. Weber, Nonlinear optimization: characterization of structural stability, *J. Global Optim.* 1 (1991) 47–64.

[27] M. Kahraman, H. Öktem, G.-W. Weber and M. Akhmet, Using piecewise linear systems with delay to grab the functional dynamics in biological systems, in *Proceedings of International Symposium on Health Informatics and Bioinformatics*, U. Sezerman (ed.), Sabanci University, 2008.

[28] P.E. Kloeden, E. Platen and H. Schurz, *Numerical Solution of SDE Through Computer Experiments*, Springer Verlag, New York, 1994.

[29] A. Kurzhanski and I. Vályi, *Ellipsoidal Calculus for Estimation and Control*, Birkhäuser, Boston, 1996.

[30] D. Lozovanu, S.W. Pickl and G.-W. Weber, Optimization, monotonicity and the determination of Nash equilibria - an algorithmic analysis, in *AIP Conference Proceedings* 718 (2004) 351–361.

[31] R.E. Moore, *Interval Analysis*, Prentice-Hall, Inc., Englewood Cliffs, N. J., 1966.

[32] R.E. Moore, *Methods and Applications of Interval Analysis*, SIAM, Philadelphia, 1979.

[33] A. Nemirovski, *Five lectures on modern convex optimization*, `http://iew3.technion.ac.il/Labs/Opt/opt/LN/Final.pdf`.

[34] A. Nemirovski, *Lectures on modern convex optimization*, Israel Institute of Technology (2002) `http://iew3.technion.ac.il/Labs/Opt/opt/LN/Final.pdf`.

[35] Y.E. Nesterov and A.S. Nemirovskii, *Interior Point Methods in Convex Programming*, SIAM, Philadelphia, 1993.

[36] S. Pickl, *Der τ-value als Kontrollparameter - Modellierung und Analyse eines Joint-Implementation Programmes mithilfe der dynamischen kooperativen Spieltheorie und der diskreten Optimierung*, thesis, Darmstadt University of Technology, Department of Mathematics, 1998.

[37] S. Pickl, Convex games and feasible sets in control theory, *Mathematical Methods of Operations Research* 53 (2001) 51–66.

[38] S. Pickl, An iterative solution to the nonlinear time-discrete TEM model - the occurence of chaos and a control theoretic algorithmic approach, *AIP Conference Proceedings* 627 (2002) 196–205.

[39] S. Pickl, An algorithmic solution for an optimal decision making process within emission trading markets, Annales du Lamsade No.3, Laboratoire d'Analyse et Modélisation de Systemes pour l'Aide a la Décision, University Lamsade, Paris, France.

[40] K. Ramadan, *Linear Programming with Interval Coefficients*, Carleton University, Ottawa, Ontario, 1996.

[41] E. Sakamoto and H. Iba, Inferring a system of differential equations for a gene regulatory network by using genetic programming, in *Proc. Congress on Evolutionary Computation*, 2001, pp. 720–726.

[42] T. Shaocheng, Interval number and fuzzy number linear programmings, *Fuzzy Sets and Systems* 66 (1994) 301–306.

[43] M. Taştan, Analysis and prediction of gene expression patterns by dynamical systems, and by a combinatorial algorithm, Institute of Applied Mathematics, METU, MSc Thesis, 2005.

[44] M. Taştan, T. Ergenç, S.W. Pickl and G.-W. Weber, Stability analysis of gene expression patterns by dynamical systems and a combinatorial algorithm, preprint, Informatics Institute, METU, Ankara (2005).

[45] M. Taştan, S.W. Pickl and G.-W. Weber, Mathematical modeling and stability analysis of gene-expression patterns in an extended space and with Runge-Kutta discretization, in *Proceedings of Operations Research*, Springer, Berlin, Heidelberg, 2005, pp. 443–450.

[46] P. Taylan and G.-W. Weber, Approximation of stochastic differential equations by additive models using splines and conic programming, in *Proceedings of CASYS'07, Eighth International Conference on Computing Anticipatory Systems*, D.M. Dubois (ed.), Liege, Belgium, 2007.

[47] P. Taylan and G.-W. Weber, New approaches to regression in financial mathematics by additive models, *Journal of Computational Technologies* 12 (2007) 3–22.

[48] P. Taylan and G.-W. Weber, Organization in finance prepared by stochastic differential equations with additive and nonlinear models and continuous optimization, *Organizacija* (Organization - Journal of Management, Information Systems and Human Resources) 41 (2008) 185–193.

[49] P. Taylan, G.-W. Weber and A. Beck, New approaches to regression by generalized additive models and continuous optimization for modern applications in finance, science and techology, *Optimization* 56 (2007) 675–698.

[50] P. Taylan, G.-W. Weber, L. Liu and F. Yerlikaya, On foundations of parameter estimation for generalized partial linear models with B-splines and continuous optimization, to appear in *Computers and Mathematics with Applications.*

[51] P. Taylan, G.-W. Weber and F. Yerlikaya, Continuous optimization applied in MARS for modern applications in finance, science and technology, in *The 20th International Conference, EURO Mini Conference " Continuous Optimization and Knowledge-Based Technologies " (EurOPT-2008)*, L. Sakalauskas, G.-W. Weber and E. K. Zavadskas (eds.), Vilnius Gediminas Technical University Publishing House "Technika ", 2008, pp. 317–322.

[52] A. Tomasgard and K.T. Midthun, Stochastic programming and natural gas - A modelling perspective,
`http://www.univie.ac.at/spxi/tutorial/TutPres_Tomasgard.pdf`

[53] Ö. Uğur, S.W. Pickl, G.-W. Weber and R. Wünschiers, An algorithmic approach to analyze genetic networks and biological energy production: an introduction and contribution where OR meets biology, *Optimization* 58 (2009) 1–22.

[54] Ö. Uğur and G.-W. Weber, Optimization and dynamics of gene-environment networks with intervals, *Journal of Industrial Management and Optimization* 3 (2007) 357–379.

[55] J. von Neumann, *Functional Operators, Vol. II. The Geometry of Orthogonal Spaces*, Princeton University Press, Princeton NJ, 1950; Ann. Math. Stud. 22, reprint of mimeographed lecture notes first distributed in 1933.

[56] G.-W. Weber, Charakterisierung struktureller Stabilität in der nichtlinearen Optimierung, in *Aachener Beiträge zur Mathematik* 5, H.H. Bock, H.T. Jongen and W. Plesken (eds.), Augustinus publishing house (now: Mainz publishing house) Aachen, 1992.

[57] G.-W. Weber, Generalized semi-infinite optimization: on iteration procedures and topological aspects, in *Similarity Methods*, B. Kröplin, S. Rudolph, S. Brückner (eds.), University of Stuttgart, 1998, pp. 281–309.

[58] G.-W. Weber, Generalized semi-infinite optimization: on some foundations, *Journal of Computational Technologies* 4 (1999) 41–61.

[59] G.–W. Weber, *Generalized Semi-Infinite Optimization and Related Topics*, Heldermann Publishing House, Research and Exposition in Mathematics 29, Lemgo, 2003.

[60] G.-W. Weber, S.Z. Alparslan-Gök and N. Dikmen, Environmental and life sciences: gene-environment networks - optimization, games and control - a survey on recent achievements, *Journal of Organisational Transformation and Social Change* 5 (2008) 197–233.

[61] G.-W. Weber, S.Z. Alparslan-Gök and B. Söyler, A new mathematical approach in environmental and life sciences: gene-environment networks and their dynamics, *Environmental Modeling & Assessment* 14 (2009) 267–288.

[62] G.-W. Weber, E. Kropat, B. Akteke-Öztürk and Z.K. Görgülü, A survey on OR and mathematical methods applied on gene-environment networks, *Cent. Eur. J. Oper. Res.* 17 (2009) 315–341.

[63] G.-W. Weber, P. Taylan, S.Z. Alparslan-Gök, S. Özöğür and B. Akteke-Öztürk, Optimization of gene-environment networks in the presence of errors and uncertainty with Chebychev approximation, in *TOP*, the Operational Research journal of SEIO (Spanish Statistics and Operations Research Society) 16 (2008) 284–318.

[64] G.-W. Weber and A. Tezel, On generalized semi-infinite optimization of genetic networks, *TOP* 15 (2007) 65–77.

[65] G.-W. Weber, A. Tezel, P. Taylan, A. Soyler and M. Çetin, Mathematical contributions to dynamics and optimization of gene-environment networks, *Optimization* 57 (2008) 353–377.

[66] G.-W. Weber, Ö. Uğur, P. Taylan and A. Tezel, On optimization, dynamics and uncertainty: a tutorial for gene-environment networks, *Discrete Applied Mathematics* 157 (2009) 2494–2513.

[67] F. Yerlikaya, G.-W. Weber, I. Batmaz, G. Köksal and P. Taylan, MARS Algoritmasında Tikhonov düzenlemesi ve çok amaçli optimizasyon kullanimi, Galatasaray University, Istanbul, Turkey, 2008.

[68] F.B. Yılmaz, A mathematical modeling and approximation of gene expression patterns by linear and quadratic regulatory relations and analysis of gene networks, Institute of Applied Mathematics, METU, MSc Thesis, 2004.

[69] F.B. Yılmaz, H. Öktem and G.-W. Weber, Mathematical modeling and approximation of gene expression patterns and gene networks, in *Operations Research Proceedings*, F. Fleuren, D. den Hertog and P. Kort (eds.), 2005, pp. 280–287.

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