SEMI-INFINITE AND CONIC OPTIMIZATION IN MODERN HUMAN, LIFE AND FINANCIAL SCIENCES UNDER UNCERTAINTY

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Abstract. In this paper, we show how advanced methods of continuous optimization contribute to modeling, learning and problem solution in areas of environmental protection, medicine and development. We begin by describing gene-environment networks under various kinds of uncertainty, the underlying Chebychev approximation to do the needed parameter estimation, and how semi-infinite optimization and conic programming come into play. We investigate the structure and stability of the topological landscape comprising these networks, present various regression models and future pathways on how computational statistics could become employed. This article widely employs systems of ordinary differential equations, but also turns to the use of stochastic differential equations which allow an elegant way to include various areas of the financial world. Our presentation analyzes important interactions between biology, health, educational and financial sectors, it introduces main results obtained by the knowledge-based technologies applied, it discusses structural frontiers, ways to overcome them, and it gives an outlook.

Keywords: Computational Biology, Environment, SIP, CQP, Uncertainty, Stability, SDE, Additive Models.

1. Introduction

Real-world data from science, technology and finance and the models describing their dynamics and relations are often influenced by uncertainty. In recent years, more sophisticated models based on interval-arithmetics were developed in order to integrate uncertainty and noise prone data of microarray experiments into so-called "gene-environment networks". In this article we address various models for gene-environment networks under uncertainty and we reveal their relation to advanced methods of continuous optimization. In addition, we indicate that this framework allows a generalization to modeling in life and financial sciences under uncertainty.

2. Gene-Expression and Environmental Data, Modeling and Dynamics

At preliminary stages of modeling, time-continuous models $\dot{E} = F(E)$ tried to imply gene-environment networks and their information. Here, $E = (E_1, \ldots, E_d)^T$ is the d-vector of positive concentration levels of proteins (or mRNAs) and environmental factors, $\dot{E}$ represents a continuous change in the gene-expression data, and $F_i : \mathbb{R}^d \to \mathbb{R}$ are nonlinear coordinate functions of F. We present a parameter estimation of unknowns implied into the definition of F, established on experimental data vectors $\overline{E}$. Since these vectors $\overline{E}$, obtained from microarray and environmental measurements, are merely approximating the actual states E at the sample times, we have $E_i = \overline{E}_i \pm Err_i$ $(i = 1, \ldots, d)$. Here, $Err_i > 0$ is some maximal measurement error likely to be made at the experimental measurements of E_i. This leads us to consider the state E_i just to be the interval $[A_i, B_i] = [\overline{E}_i - Err_i, \overline{E}_i + Err_i]$ and, hence, $E = (E_1, \ldots, E_d)^T$ to be in the d-dimensional parallelpipe $\prod_{i=1}^{d} [A_i, B_i]$. This approach recently introduced for gene-environment networks (Weber, 2007cd) allows us to approximately address the nature of biological, environmental and technical phenomena of measurement and modeling as well. It extends the one from (Gebert, 2006; Gebert, 2007) to the continuous equation (CE) $\dot{E} = M(E)E$, $E(t_0) = E^{(0)}$. Here, $M(E)$ is a $(d \times d)$-matrix whose entries are intervals defined by a family of functions which include unknown parameters. Now, intervals represent uncertainty with respect to the interactions between the genes, to the effects between the environment and the genes, or between environmental items.

3. Two Levels of the Parametric Task

Referring to the parametrized entries, a *bilevel problem* of two different problem stages can be distinguished, namely, optimization and stability analysis:

(I) The *optimization (approximation) problem* of squared errors bases on the form

$$\min_y \sum_{\kappa=0}^{l-1} \left\| M_y\!\left(\overline{E}^{(\kappa)}\right)\overline{E}^{(\kappa)} - \dot{\overline{E}}^{(\kappa)} \right\|_\infty^2,$$ where the vector y comprises a first subset of all the

parameters. The vector $\dot{\overline{E}}^{(\kappa)}$ consists of interval-valued *difference quotients* raised on the κth experimental data $\overline{E}^{(\kappa)}$ and on step lengths $\overline{h}_\kappa = \overline{t}_{\kappa+1} - \overline{t}_\kappa$. Since we turned to an interval-valued setting, we inserted the *Chebychev norm* $\|\cdot\|_\infty$ generating the topology of uniform convergence (cf. Section 4). Thus, we turned from *discrete* (Gaussian, least-squares) approximation and nonlinear optimization (Gebert, 2007) to *uniform* (Chebychev) approximation and semi-infinite optimization (Uğur, 2007; Weber, 2006cd).

(II) *Stability of the dynamics* is investigated with respect to the remaining parameters. For this a combinatorial algorithm on polyhedra sequences observed is used to detect the regions of stability. Indeed, (CE) allows a time-discretization (DE) $E^{(k+1)} = M^{(k)} E^{(k)}$, where

$$M^{(k)} = I + \frac{h_k}{2} M(E^{(k)}) + \frac{h_k}{2} M(E^{(k)} + h_k M(E^{(k)}) E^{(k)})(I + h_k M(E^{(k)})),$$ by Heun's Method.

Therefore, the kth approximation $\hat{E}^{(k)}$ can be calculated by the matrix-multiplication $\hat{E}^{(k)} = M^{(k-1)}(M^{(k-2)}\ldots(M^{(1)}(M^{(0)} E^{(0)})))$, $k \in \mathrm{IN}$. Based on this recursion, a stability analysis of combinatorial and geometrical type with polytope series is permitted (Gebert, 2006). Furthermore, via (DE) we obtain our *gene-environment networks* by the time-discrete dynamics (while our investigation permits a time-continuous approach to the networks via (CE), too). Indeed, the genes and environmental items are represented by the nodes (vertices) of our network; the interactions between them turn to edges weighted with effects (in the time-continuous case: with functional values). Thus, at each discrete time step $k \mapsto k+1$ the expression level of gene i becomes changed by the jth gene (or ℓth environmental item).

4. Extracting and Optimizing Gene-Environment Networks in the Presence of Intervals

In (Gebert, 2007), a hybrid approach has been presented which offers a complete dynamical description of the expression levels of n genes. Then, the contributions (Uğur, 2007; Weber, 2007bc) modified it by additionally matching the n genes with m special items and the cumulative item of the environment, and by turning to the interval-valued setting:

$$\dot{E}(t) = M_{s(t)} E(t) + W_{s(t)} \breve{E}(t) + V_{s(t)}, \text{ with}$$
$$Q(E(t)) = (Q_1(E(t)), Q_2(E(t)), \ldots, Q_d(E(t))), \text{ where}$$
$$Q_i(E(t)) = \begin{cases} 0, & E_i(t) < \theta_{i,1} \\ 1, & \theta_{i,1} \le E_i(t) < \theta_{i,2} \\ \vdots \\ d_i, & \theta_{i,d_i} \le E_i(t) \end{cases} \quad (i = 1, 2, \ldots, n). \tag{HE}$$

In (HE), $\theta_{i,1} < \theta_{i,2} < \ldots < \theta_{i,d_i}$ are thresholds of the expression levels where instantaneous changes of the parameter constellation can occur; $\breve{E}(t) = \left(\breve{E}_1(t), \ldots, \breve{E}_m(t)\right)^T$ is a specific m-vector (of intervals) which comprises the levels of the m environmental factors, $M_{s(t)}$, $W_{s(t)}$ are matrices of

the type $n \times n$ and $n \times m$, respectively, and $V_{s(t)}$ is an n-vector (all three ones over intervals). The function $Q : \mathbb{R}^n \to \mathrm{IN}_0^n$ implies the threshold constellation, and $s(Q(E))$ indicates where in the state space the system is placed at E, and which matrices and vectors M, W, V have to be chosen to specify the system such that the given data are approximated best. The function $s : \mathrm{IN}_0^n \to \mathrm{IN}_0$ must be injective, such that a different triplet (M, W, V) is used whenever a threshold is traversed. This *piecewise linear* approach provides an approximation of the global nonlinearity of nature and the system (HE) can indeed be generalized such that the matrices and vectors depend on E, then, the involved parameters are affected, governed and instantaneously changed via $s(t)$. For the parameter estimation of (HE), we require (I) an *estimation of the thresholds* $\theta_{i,j}$ (e.g., by *Akaike's Information Criterion* (Gebert, 2007)) and (II) an *calculation of the matrices and vectors* $M_{s(t)}$, $W_{s(t)}$ and $V_{s(t)}$, which are describing the system in between the thresholds. The gene-expression levels are compact intervals such that the vectors E are parallelpipes, all of them lying in a sufficiently large parallelpipe P. Via canonical projections, the thresholds define a partition of P into subparallelpipes (regimes) $P^{*,\rho} \subset P$ ($\rho \in \{1, 2, \ldots, \ell\}$), where $\ell = \prod_{i=1}^n (d_i + 1)$. For any given subparallelpipe $P^* = P^{*,\rho}$ we have to extract the parametric unknowns $M_{s(t)}$, $W_{s(t)}$ and $V_{s(t)}$ from given data. In P^*, the hybrid system (HE) reduces to a system of ordinary linear differential equations. Hence, we can find analytical solutions for the corresponding parts of the state space.

5. Mixed-Integer Parameter Estimation

Minimization of the quadratic error between the difference quotients $\dot{\bar{E}}^{(\kappa_\alpha)}$ and the right-hand side of the differential equations evaluated at the finitely many measurement intervals $\bar{E}^{(\kappa_\alpha)} \in P^*$ ($\alpha = 0, \ldots, l^* - 1$) turns to the *generalized Chebychev approximation problem*

$$\min_{(m_{ij}^*),(W_{i\ell}^*),(V_i^*)} \sum_{\alpha=0}^{l^*-1} \left\| M^* \bar{E}^{(\kappa_\alpha)} + W^* \bar{\bar{E}}^{(\kappa_\alpha)} + V^* - \dot{\bar{E}}^{(\kappa_\alpha)} \right\|_\infty^2. \tag{HLS}$$

Since it can equivalently be written as a semi-infinite optimization problem (Weber, 2007bd), we get access to the applicable methodology of SIP.

Real-world gene-environment networks are huge, such that for practical reasons we have to rarefy them by diminishing the number of arcs (Uğur, 2007; Weber, 2007b). Therefore, upper bounds on the outdegrees of nodes are introduced. We define the Boolean matrices and vectors, $X = (\chi_{ij})_{i,j=1,\ldots,n}$, $\Xi = (\xi_{i\ell})_{\substack{i=1,\ldots,n \\ \ell=1,\ldots,m}}$ and $Z = (\varsigma_i)_{i=1,\ldots,n}$, representing by the values 1 and 0 whether or not gene j regulates gene i, environmental item ℓ regulates gene i and the environment cumulatively regulates gene i. Hence, the *outdegrees* $\sum_{i=1}^n \chi_{ij}$, $\sum_{i=1}^n \xi_{i\ell}$ and $\sum_{i=1}^n \varsigma_i$ count the numbers of genes regulated by gene j, by environmental item ℓ or by the cumulative environment, respectively. Our network rarefaction by bounding the outdegrees obeys the principles of least-squares. We also imply any helpful *a priori* knowledge into the problem (degradation rates, connectedness structure). Herewith, our parameter estimation task becomes a (generalized) *mixed-integer Chebychev approximation problem*:

$$\min_{(m_{ij}^*),(W_{i\ell}^*),(V_i^*),(\chi_{ij}),(\xi_{i\ell}),(\varsigma_i)} \sum_{\alpha=0}^{l^*-1} \left\| M^* \bar{E}^{(\kappa_\alpha)} + W^* \bar{\bar{E}}^{(\kappa_\alpha)} + V^* - \dot{\bar{E}}^{(\kappa_\alpha)} \right\|_\infty^2 \tag{MICP}$$

subject to $\quad \sum_{i=1}^n \chi_{ij} \le \alpha_j, \ \sum_{i=1}^n \xi_{i\ell} \le \beta_\ell, \ \sum_{i=1}^n \varsigma_i \le \gamma, \ m_{ii}^* \ge \delta_{i,\min} \quad (i, j = 1, 2, \ldots, n, \ \ell = 1, 2, \ldots, m)$.

6. Improved Modeling by GSIP Extension

Prepared by (Weber, 2007bcd; Uğur, 2007), we use continuous optimization for a "softening" of (MICP) by replacing the binary variables χ_{ij}, $\xi_{i\ell}$ and ζ_i with real variables p_{ij}, $q_{i\ell}$, $r_i \in [0,1]$ which linearly depend on the elements of m_{ij}, $w_{i\ell}$ and v_i (also interpretable as probabilities). For the latter ones we assume some reasonable box constraints. Herewith, the values $\Sigma_{j=1}^{n} p_{ij}(m_{ij}^*)$, $\Sigma_{i=1}^{m} q_{i\ell}(w_{i\ell}^*)$ and $\Sigma_{i=1}^{m} r_i(v_i^*)$ have become interval-valued approximations of the numbers of genes regulated by gene j, environmental item ℓ and cumulative environment. Having solved the continuous optimization problem, we could return the binary variables and, hence, network rarefaction, by staying below some small prescribed values $\varepsilon_{ij}, \varepsilon_{i\ell}, \varepsilon_i \in [0,1)$. The environment can affect the connectedness between the genes and an external stimulus may activate a higher regulation. Therefore, we 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 $w_{i\ell}^* e_{m(i-1)+\ell}$ and $v_i^* e_{mn+i}$:

$$Y(V^*, W^*) = conv\left(\left\{ w_{i\ell}^* e_{m(i-1)+\ell} \,\middle|\, i=1,\ldots,n; \ell=1,\ldots,m \right\} \cup \left\{ v_i^* e_{mn+i} \,\middle|\, i=1,\ldots,n \right\}\right)$$
$$= \left\{ \sum_{\substack{i=1,\ldots,n \\ \ell=1,\ldots,m}} \sigma_{i\ell} w_{i\ell}^* e_{m(i-1)+\ell} + \sum_{i=1,\ldots,n} \sigma_{i,m+1} v_i^* e_{mn+i} \,\middle|\, \sigma_{i\tau} \geq 0 (i=1,\ldots,n; \tau=1,\ldots,m+1), \sum_{\substack{i=1,\ldots,n \\ \tau=1,\ldots,m+1}} \sigma_{i\tau} = 1 \right\}$$

where e_η is the $((m+1)n)$- dimensional unit vector. Formally, we can write $Y(V^*, W^*)$ as a parallelpipe. Now, we get our (generalized) *relaxed Chebychev approximation problem*:

$$\min_{(m_{ij}^*),(W_{i\ell}^*),(V_i^*)} \sum_{\alpha=0}^{\ell^*-1} \left\| M^* \overline{E}^{(\kappa_\alpha)} + W^* \overline{\overline{E}}^{(\kappa_\alpha)} + V^* - \dot{E}^{(\kappa_\alpha)} \right\|_\infty^2 , \qquad \text{(RCP)}$$

subject to $\Sigma_{i=1}^{n} p_{ij}(m_{ij}^*, y) \leq \alpha_j(y)$, $\Sigma_{i=1}^{m} q_{i\ell}(w_{i\ell}^*, y) \leq \beta_\ell(y)$, $\Sigma_{i=1}^{m} r_i(v_i^*, y) \leq \gamma(y)$ $\quad (y \in Y(V^*, W^*))$,

$$\delta_{i,\min} \leq m_{ii}^*, \; \underline{m}_{ij}^* \leq m_{ij}^* \leq \overline{m}_{ij}^*, \; \underline{w}_{i\ell}^* \leq w_{i\ell}^* \leq \overline{w}_{i\ell}^*, \; \underline{v}_i^* \leq v_i^* \leq \overline{v}_i^* \qquad (i,j=1,\ldots,n; \ell=1,\ldots,m).$$

Firstly, we compare m_{ii}^* and $\delta_{i,\min}$, then, take the largest of the two values as a single lower bound instead ($\delta_{i,\min} < \overline{m}_{ii}^*$ provided). As given in the objective function by generalized Chebychev approximation, this uniform interpretation of the "$\leq$" conditions amounts to the SIP character of (RCP). By the additional coupling of our inequality constraint set $Y(V^*, W^*)$ with the states (V^*, W^*), (RCP) even becomes a GSIP problem. In the objective function, the terms with the κ th Chebychev norm are nonsmooth max-type functions, but also a smooth modeling is possible.

7. On GSIP and Structural Stability for Gene-Environment Networks

GSIP applied for our gene-environment problem (RCP), reveals the general program form

$$P_{GSI}(f,h,g,u,v) \begin{cases} \text{minimize } f(x) \text{ on } M_{GSI}[h,g], \text{where} \\ M_{GSI}[h,g] = \left\{ x \in \mathbb{R}^d \,\middle|\, h_i(x)=0 \; (i \in I), g^j(x,y) \geq 0 (y \in Y^j(x), j \in J) \right\} \end{cases} \qquad \text{(A}_1\text{)}$$

with finite I, J and *finitely constrained (F)* feasible sets $Y^j = Y^j(x)$. For each $x \in \mathbb{R}^d$, we have

$$Y^j(x) = M_F[u^j(x,\cdot), v^j(x,\cdot)] = \{ y \in \mathbb{R}^q \,|\, u_k(x,y)=0 \; (k \in K^j), v_\ell(x,y) \geq 0 \; (\ell \in L^j) \} \qquad \text{(A}_2\text{)}$$

with finite sets K^j and L^j. The model (A_1)-(A_2) allows equality constraints on both the upper (x-) level and lower (y-) level representing, e.g., metabolic or financial restrictions, reactions or balance equations. The outdegree constraints in (RCP) may be assumed to be of class C^2, too. The bounds guarantee that the feasible set $M_{GSI}[h,g]$ 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 (Weber, 2003)). Here, the sets $Y^j(x)$ are compact and they fulfill the *Linear Independence Constraint Qualification* (*LICQ*), an appropriate choice of the overall box constraints provided. The works (Weber, 2003; Weber, 2007b; Uğur, 2007) provide more detailed discussions and generalizations of GSIP.

8. Stability Theory

Perturbations $(f, h, g, u, v) \mapsto (\tilde{f}, \tilde{h}, \tilde{g}, \tilde{u}, \tilde{v})$ of our gene-environment networks are caused, e.g., as follows (Weber, 2007c): (I) Outliers of parallelpipes: We can face them by multiplying some dampening factor on the corresponding squared error. (II) The data of a measurement gives rise to one optimization problem and network so that the data of a subsequent measurement can be viewed as a "perturbed" problem and network. Finally, our entire interval-valued modeling has been representing perturbations of (III) errors, imprecision and uncertainty. The *strong Whitney topology* C_S^2 serves as a "measure" of perturbations so that asymptotic aspects are taken into account. The "genetic (and environmental) fingerprint" of (RCP) is given by all the lower level sets of its objective function. If the perturbed and the arbitrarily slightly unperturbed lower level sets are homeomorphic to each other, under some correspondence between the levels, we call (RCP) *structurally stable* (Weber, 2003). Our main theorem states that structural stability can just be *characterized* by two well-known regularity conditions and a more technical one (Weber, 2007cd):

Characterization Theorem on Structural Stability for Gene-Environment Networks:
The optimization problem $P_{GSI}(f, h, g, u, v)$ on gene-environment networks is *structurally stable*, if and only if the following triplet of conditions $C_{1,2,3}$ is satisfied:

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

C_2 All the G-O Kuhn-Tucker points $\bar{x}$ of $P_{GSI}(f, h, g, u, v)$ are (G-O)-strongly stable.

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

This theorem helps for an understanding of the "landscape" of gene-environment networks, for their perturbational behaviour and for the development of numerical procedures. We can consider "mountain paths" (saddles) between any two candidate networks being given by local minimizers of (RCP). All the points around candidate solutions can be regarded as potential networks which may be obtained after perturbations (Weber, 2003). 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 governed by the steepness of the function around the solution. If a local or global minimizer is very steep, we can associate this with stability, whereas flatness is related with instability (Weber, 2007d). For a better analytical understanding of (RCP), we identify possible pathologies in terms of one or more of the conditions $C_{1,2,3}$ violated. We point out a relation to *conic programming* (CP), however, in a GSIP sense. If in (RCP) all the functions defining the constraints are linear and the squares on the Chebychev norms deleted, then we obtain 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). In CP problems, *interior point methods* can be introduced and efficiently applied.

9. Applications in Finance and Technology

The models presented in the previous sections have been successfully applied to various problems from finance and technology. As example, we mention the *Technology-Emissions-model* (TEM-Model) of S.W. Pickl for the simulation of a complex cooperative economic behaviour of countries/enterprises in order to reduce *CO_2-emissions* and to alleviate the effects of *global warming* as mentioned in the *Kyoto Protocol* (Pickl, 1998). In (Weber, 2007a), an interval-valued model reformulation of the TEM-model in the framework of our gene-environment networks was presented, incorporating data from finance, technology and emissions under uncertainty. Besides the models presented in the previous sections, *additive models* based on *spline regression* were considered. This approach even allows an approximation by *stochastic differential equations* $dX_t = a(X_t,t)dt + b(X_t,t)dW_t$, with regard to the Wiener process W_t, drift term a and diffusion b, being a platform of continuous and future improvements of our model and results (Taylan, 2007).

10. Conclusions

In this paper, we surveyed the work done by us with our colleagues in modeling, optimization, and dynamical representation of the patterns of genetic, environmental and also financial information. We presented several models of gene-environment networks under uncertainty and pointed out their relation to various kinds of optimization. For a deep understanding of the topological landscape of gene-environment networks determined by that optimization, we stated a characterization result on structural stability, and we related to conic quadratic programming. We also indicated the relations of our methodology to applications in finance and technology.

References

Gebert, J., Lätsch, M., Pickl, S.W., Weber, G.-W., Wünschiers, R. (2006) "An algorithm to analyze stability of gene-expression pattern", in Anthony, M., Boros, E., Hammer, P.L., Kogan, A. (guest eds.), special issue *Discrete Mathematics and Data Mining II* of Discrete Applied Mathematics 154, 7, pp. 1140-1156.

Gebert, J., Radde, N., Weber, G.-W. (2007) "Modelling gene regulatory networks with piecewise linear differential equations", to appear in the special issue (feature cluster) *Challenges of Continuous Optimization in Theory and Applications* of European Journal of Operational Research 181, 3, pp. 1148-1165.

Pickl, S.W. (1998) "Der $\tau-$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.

Taylan, P., Weber, G.-W. (2007) "Approximation of stochastic differential equations by additive models using splines and conic programming", submitted to the proceedings of CASYS'07, Liege, Belgium, August 6-11, 2007.

Uğur, Ö., Weber, G.-W. (2007) "Optimization and dynamics of gene-environment networks with intervals", in the special issue at the occasion of the 5th Ballarat Workshop on Global and Non-Smooth Optimization: Theory, Methods and Applications, November 28-30, 2006, of Journal of Industrial Management and Optimization 3, 2 (May 2007) pp. 357-379.

Weber, G.-W. (2003), Generalized Semi-Infinite Optimization and Related Topics, Heldermann Publishing House, Research and Exposition in Mathematics 29, Lemgo.

Weber, G.-W., Alparslan-Gök, S.Z., Söyler, B. (2007a) "A new mathematical approach in environmental and life sciences: gene-environment networks and their dynamics", preprint, Institute of Applied Mathematics, METU, 2006, invited paper submitted to Environmental Modeling & Assessment.

Weber, G.-W., Tezel, A., Taylan, P., Soyler, A., Çetin, M. (2007b) "On dynamics and optimization of gene-environment networks", preprint, to appear in the special issue of Optimization in honour of the 60th birthday of Prof. Dr. H.Th. Jongen.

Weber, G.-W., Taylan, P., Alparslan-Gök, Z., Özöğür, S., Akteke-Öztürk, B. (2007c) "Optimization of gene-environment networks in the presence of errors and uncertainty with Chebychev approximation", preprint, Institute of Applied Mathematics, METU, submitted to TOP.

Weber, G.-W., Uğur, Ö., Taylan, P., Tezel, A. (2007d) "On optimization, dynamics and uncertainty: a tutorial for gene-environment networks", to appear in the special issue of Discrete Applied Mathematics *Networks in Computational Biology*.