Nature-Inspired Metaheuristic Algorithms for Finding Efficient Experimental Designs

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University of Georgia
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Two Upcoming Statistics Conferences at UCLA

- Western Northern American Region (WNAR 2013)
  June 16-19 2013
  http://www.wnar.org

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- Close to the Pacific Ocean

Acknowledgements of Collaborators

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Outline

1. Motivation

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- Issues - proof, speed of convergence, ease of use and availability of software
- Is there an easy-to-use and efficient method for finding optimal designs for different types of optimal designs for any given model?

1.1 Locally D-optimal Designs for the Logistic Model on $X = [-1, 1]$ (from Silvey's text, 1980)

$$log \frac{\pi(x)}{1-\pi(x)} = \theta_1 + \theta_2 x, \quad \theta \in \Theta = \{(\theta_1, \theta_2) : \theta_1 > 0 \ \& \ \theta_2 > 0\}.$$

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- Let a^* solve $exp(a) = (a+1)/(a-1)$ and let u^* solve

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-

condition	locally D-optimal design
$\{\theta : \theta_2 - \theta_1 \geq a\}$	$\{\frac{a-\theta_1}{\theta_2}, \frac{-a-\theta_1}{\theta_2}; \frac{1}{2}, \frac{1}{2}\}$
$\{\theta : \theta_2 - \theta_1 < a, exp(\theta_1 + \theta_2) \leq \frac{\theta_2+1}{\theta_2-1}\}$	$\{-1, u^*; \frac{1}{2}, \frac{1}{2}\}$
$\{\theta : exp(\theta_1 + \theta_2) > \frac{\theta_2+1}{\theta_2-1}\}$	$\{-1, 1; \frac{1}{2}, \frac{1}{2}\}$

1.2 Amended Ford's results on $X = [-c, c],\ c > 0$

Let a^* solve the equation $e^a = \frac{a+1}{a-1}$ $\qquad (a^* = 1.5434)$,

let b^* solve the equation $e^{\theta_0 + bc} = \frac{cb+1}{cb-1}$

and let x^* solve the equation $e^{\theta_0+\theta_1 x} = \frac{(x+c)\theta_1+2}{(x+c)\theta_1-2}$.

condition	locally D-optimal design
$\{\theta : \theta_1 > \frac{1}{c}(\theta_0 + a^*)\}$	$\{\frac{-a^*-\theta_0}{\theta_1}, \frac{a^*-\theta_0}{\theta_1}; \frac{1}{2}, \frac{1}{2}\}$
$\{\theta : b^* < \theta_1 \leq \frac{1}{c}(\theta_0 + a^*)\}$	$\{-c, x^*; \frac{1}{2}, \frac{1}{2}\}$
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- Corrected results when $X = [a, b]$ in Sebastiani and Settimi (JSPI, 1997)
- What is the E-optimal design for $X = [3, 6]$?

1.3 A 4-parameter Heteroscedastic Hill Model

$$y_i = \frac{(E_{con} - b)(\frac{D_i}{IC_{50}})^m}{1 + (\frac{D_i}{IC_{50}})^m} + b + \varepsilon_i = \eta(D_i, \theta) + \varepsilon_i, \ \ \varepsilon_i \sim N(0, \sigma(Ey_i)^{2\lambda})$$

D_i = dose of a drug assigned to subject i

y_i = drug effect of subject i

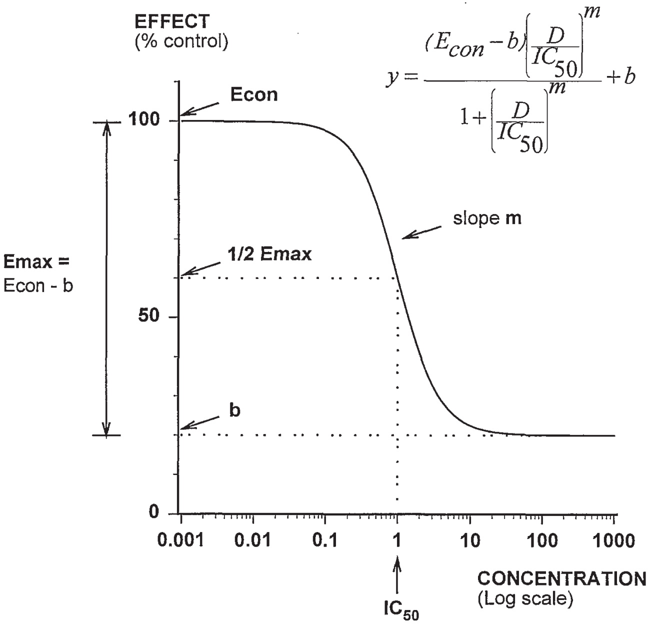
E_{con} = the control effect at zero drug concentration

b = background effect at infinite drug concentration

IC_{50} = inflection point on the curve (a measure of the drug potency)
= drug concentration that induces a 50% decrease in the maximal effect ($Econ - b$)

m = slope parameter of the curve.

1.4 Selected Plot of the Mean Function



1.5 Information matrix for the Hill Model

Let the nominal value for θ be $\theta_0 = (E_{con}^0, b^0, IC_{50}^0, m^0)^T$ and let

$$f^T(x,\theta_0) = \left(\frac{\partial\eta(x,\theta)}{\partial E_{con}}, \frac{\partial\eta(x,\theta)}{\partial b}, \frac{\partial\eta(x,\theta)}{\partial IC_{50}}, \frac{\partial\eta(x,\theta)}{\partial m}\right)\Big|_{\theta_0}$$

$$\begin{aligned} \textit{where} \quad \frac{\partial\eta(x,\theta)}{\partial E_{con}} &= \frac{(x/IC_{50})^m}{(1+x/IC_{50})^m} \\ \frac{\partial\eta(x,\theta)}{\partial b} &= \frac{1}{1+(x/IC_{50})^m} \\ \frac{\partial\eta(x,\theta)}{\partial IC_{50}} &= -\frac{(b-E_{con})(x/IC_{50})^m \log(x/IC_{50})}{(1+(x/IC_{50})^m)^2} \\ \frac{\partial\eta(x,\theta)}{\partial m} &= \frac{(b-E_{con})m(x/IC_{50})^m}{IC_{50}(1+(x/IC_{50})^m)^2}. \end{aligned}$$

The total information matrix is proportional to

$$M(\xi,\theta_0) = F^T W F$$

where $F = \left[f^T(x_1), f^T(x_2), \ldots f^T(x_n)\right]^T$ and $W = diag(y_1^{-2\lambda}, ..., y_n^{-2\lambda})$.

1.6 Algorithms and Their Usage (Whitacre, 2011)

(a) Recent trends indicate rapid growth of nature-inspired optimization in academia and industry. Computing, Vol. 93, 121-133.
(b) Survival of the flexible: explaining the recent dominance of nature-inspired optimization within a rapidly evolving world. Computing, Vol. 93, 135-146.

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- Compared different types of algorithms based on historical bias, academic bias, conceptual appeal, simplicity of implementation, algorithm utility, flexibility
- NNIM = { greedy randomized adaptive search, great deluge, squeaky wheel optimization, tabu, harmony search, unit-walk, stochastic local search, iterated greedy algorithms, iterated local search, cross entropy method, extremal optimization, stochastic diffusion search, reactive search optimization, random-restart hill climbing, variable neighborhood search }

1.7 Mathematical Optimization Techniques (MOT) versus Nature-Inspired Metaheuristics (NIM)

- MOT = { mathematical programming, constraint programming,quadratic programming, quasi-Newton method, nonlinear programming, interior-point method, goal programming, integer programming, simplex method, branch and bound algorithm, linear programming, dynamic programming, branch-and-cut, exhaustive search, branch and price, convex programming, stochastic programming,quasi-convex programming}

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- NIM = { genetic algorithm, evolutionary computation, swarm optimization, ant colony optimization, memetic algorithm, genetic programming, simulated annealing, nature inspired algorithm, bio-inspired optimization, evolutional strategies, swarm intelligence, hyper-heuristics, adaptive operator selection, multi-meme algorithms, self generating algorithms, honey bees algorithm, differential evolution}

2. Metaheuristic Algorithms

From Wikipedia, the free encyclopedia: Meta-heuristic

In computer science, meta-heuristic designates a computational method that optimizes a problem by iteratively trying to improve a candidate solution with regard to a given measure of quality. Meta-heuristics make few or no assumptions about the problem being optimized and can search very large spaces of candidate solutions. However, meta-heuristics do not guarantee an optimal solution is ever found. Many meta-heuristics implement some form of stochastic optimization.

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- Our interest here is nature-inspired meta-heuristic algorithms
- Particle Swarm Optimization (PSO) proposed by Eberhard & Kennedy (IEEE, 1995) models animal instincts.

2.1 Heuristics versus Metaheuristics

Taken from stackoverflow.com/questions/10445700/what-is-the-difference-between-heuristics-and-metaheuristics

Heuristics are often problem-dependent, that is, you define and heuristic for a given problem. Meta-heuristics are problem-independent techniques that can be applied to a broad range of problems. A meta-heuristic knows nothing about the problem it will be applied, it can treat functions as black boxes.

A heuristic exploits problem-dependent information to find a ’good enough’ solution to a specific problem, while meta-heuristics are, like design patterns, general algorithmic ideas that can be applied to a broad range of problems.

Particle swarm optimization: Origins

How can birds or fish exhibit such a coordinated collective behavior?

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- International Conference on Swarm Intelligence: Theoretical Advances and Real world Applications in France on June 2011
- A journal, Swarm Intelligence, was born in 2007 and another, International Journal of Swarm Intelligence Research, in 2010 - just to keep track of PSO development and applications in the real world. A third is Swarm and Evolutionary Computation (2011)

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- reactive power and voltage control in electric power systems

2.5 Recent Papers in Particle Swarm Optimization

Parameter Estimation of Nonlinear Econometric Models using PSO. Ekonomicka Revue-Central European Review of Economic Issues (2010).

A Novel Global Search Algorithm for Nonlinear Mixed-Effects Models using PSO. J. of Pharmacokinetics Pharmacodynamics (2011).

Optimizing Latin Hypercube Designs by PSO. Statistical Computing. (2013).

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- Paterlini, S. and Krink, T. (2006). Differential Evolution and PSO in Partitional Clustering. Computational Statistics and Data Analysis, 50, 1220-1247.

2.6 Main Features of PSO:

Random generation of an initial population

Each particle has a fitness value that depends on the optimum

Population is reproduced based on fitness value

If requirements are met, stop; otherwise each particle updates its fitness value

Shares similarity with genetic algorithm but differs in important ways discussed in numerous sites such as http://www.alife.org or http://www.engr.iupui.edu/ eberhart with tutorials

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- PSO comprises a very simple concept, its paradigms can be implemented in a few lines of computer code, requires only primitive mathematical operators and is computationally inexpensive in terms of both memory requirement and speed

2.7 Basic Equations and tuning parameters in PSO

$$\mathbf{v_i}(t+1) = \omega_i \mathbf{v_i}(t) + c_1\beta_1(\mathbf{p_i}(t) - \mathbf{x_i}(t)) + c_2\beta_2(\mathbf{p_g}(t) - \mathbf{x_i}(t)),$$
$$\mathbf{x_i}(t+1) = \mathbf{x_i}(t) + \mathbf{v_i}(t+1).$$

x_i and v_i: position and velocity for the ith*particle*

β_1 and β_2: random vectors

ω_i: inertia weight that modulates the influence of the former velocity

c_1 and c_2: cognitive learning parameter and social learning parameter

p_i and p_g: Best position for the i^{th} particle (local optimal) and for all particles (global optimal)
For many applications, $c_1 = c_2 = 2$ seem to work well and usually $20 - 50$ particles will suffice (Kennedy, IEEE, 1997).

3 Demonstrations: PSO-generated Optimal Designs

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3.1 Locally D-optimal Designs for a 4-parameter Hill Model

3.2 Locally D-Optimal Designs for a Rational Polynomial Model

3.3 Optimal Designs for a Continuation Ratio Model

3.4 Locally c-Optimal Designs for a Compartmental Model

3.5 Locally D_s-optimal Designs for the Quadratic Logistic Model

- 3.6 Minimax Optimal Designs: Background

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- Minimax D-optimal Designs for the Logistic Model

3.1: PSO-generated designs coincide with the locally D-optimal designs for the Hill model with fixed nominal values $E_{con} = 1.7,\ b = 0.137, \lambda = 0.794$ and various nominal values for IC_{50} and m for different drugs:

Drug	IC_{50}	m	support points			
TMTX	0.00875	-1.790	0	0.00773	0.02965	8.95
MTX	0.0223	-2.740	0	0.02056	0.04950	22.3
AG2034	0.453	-0.825	0	0.32042	5.56703	453
AG2032	0.0774	-3.490	0	0.07263	0.144756	77.4
AG2009	111	-1.030	0	53.9007	377.2057	1500
AG337	0.468	-1.540	0	0.40495	1.93184	468
ZD1694	0.0429	-1.690	0	0.03761	0.15624	42.9

Reference: Khinkis el at. (2003). Optimal Design for Estimating Parameters of the 4-parameter Hill Model. Nonlinearity in Biology, Toxicology and Medicine, Vol.1, 363-377.

3.2 Locally D-Optimal Designs for a Rational Polynomial Model

The model is

$$E(y) = \frac{x+\alpha}{\beta_0 + \beta_1(x+\alpha) + \beta_2(x+\alpha)^2}$$

Examples of the equally weighted locally D-optimal designs:

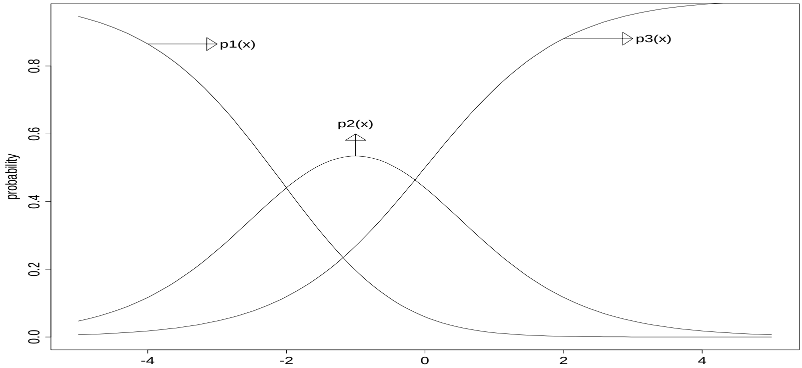
	nominal values				support points			
Case	α	β_0	β_1	β_2				
(i)	0.1	1.0	-0.8	1	0	0.384	0.964	2.424
(ii)	0.5	1.0	0.8	1	0	0.302	1.285	5.470

Cobby, J. M., Chapman, P. F. and Pike, D. J. (1986). Design of Experiments for Estimating Inverse Quadratic Polynomial Responses, Biometrics, 42, 659 – 664.

The Continuation Ratio Model relates probabilities of no response (p_1),efficacy and no severe toxicity (p_2) and severe toxicity (p_3) by:

$$\ln[p_3(\theta,x)/(1-p_3(\theta,x))] = a_1 + b_1 x, \quad b_1 > 0 \quad (1)$$

$$\ln[p_2(\theta,x)/p_1(\theta,x)] = a_2 + b_2 x, \quad b_2 > 0. \quad (2)$$



Example 3.3a: Calculus

The biologically optimal dose x_{BOD} depends on $\theta^T = (a_1, b_1, a_2, b_2)$ and solves

$$g(x, \theta) = b_2(1 + e^{-a_1 - b_1 x}) - b_1(1 + e^{a_2 + b_2 x}) = 0.$$

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- By the implicit function theorem, the gradient of the solution to the above equation is

$$\left[\frac{\partial g(x_{BOD}(\theta), \theta)}{\partial x}\right]^{-1} \frac{\partial g(x_{BOD}(\theta), \theta)}{\partial \theta}$$
$$= \begin{pmatrix} e^{-a_1 - b_1 x_{BOD}} / [b_1(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ x_{BOD} e^{-a_1 - b_1 x_{BOD}} / [b_1(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ e^{a_2 + b_2 x_{BOD}} / [b_2(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ x_{BOD} e^{a_2 + b_2 x_{BOD}} / [b_2(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \end{pmatrix}.$$

Example 3.3a: Calculus

The biologically optimal dose x_{BOD} depends on $\theta^T = (a_1, b_1, a_2, b_2)$ and solves

$$g(x,\theta) = b_2(1 + e^{-a_1 - b_1 x}) - b_1(1 + e^{a_2 + b_2 x}) = 0.$$

- By the implicit function theorem, the gradient of the solution to the above equation is

$$\left[\frac{\partial g(x_{BOD}(\theta),\theta)}{\partial x}\right]^{-1} \frac{\partial g(x_{BOD}(\theta),\theta)}{\partial \theta}$$
$$= \begin{pmatrix} e^{-a_1 - b_1 x_{BOD}} / [b_1(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ x_{BOD} e^{-a_1 - b_1 x_{BOD}} / [b_1(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ e^{a_2 + b_2 x_{BOD}} / [b_2(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \\ x_{BOD} e^{a_2 + b_2 x_{BOD}} / [b_2(e^{-a_1 - b_1 x_{BOD}} + e^{a_2 + b_2 x_{BOD}})] \end{pmatrix}.$$

- Use standard algorithm to generate the locally optimal design

3.3b Selected BOD- & D-optimal designs and D-efficiencies (Fan & Chaloner, JSPI, 2003)

dose	weight	(a_1, b_1, a_2, b_2)	dose	weight	D-efficiency
-5.67	0.001	$(-3.3, 0.5, 3.4, 1)$	-4.63	0.292	56%
-0.64	0.800		-1.32	0.416	
4.84	0.199		4.19	0.056	
			8.64	0.236	
-1.26	0.632	$(-1, 0.5, 2, 1)$	-3.54	0.366	67%
4.11	0.368		-0.59	0.403	
			4.80	0.231	
-1.30	0.549	$(-1.04, 0.81.2, 1)$	-2.67	0.370	77%
2.37	0.451		0.00	0.398	
			2.88	0.232	
-14.00	0.100	$(0.4, 0.2, 2, 1)$	-13.00	0.070	62%
-1.14	0.628		-4.11	0.400	
9.99	0.272		-0.77	0.372	
			9.08	0.158	

3.4 A 3-parameter Compartment Model

A popular compartmental model with $\theta^T = (\theta_1, \theta_2, \theta_3)$:

$$\eta(x,\theta) = \theta_3\{exp(-\theta_2 x) - exp(-\theta_1 x)\} \quad \theta_1 \geq \theta_2 \geq 0, \theta_3 \geq 0, \quad x \geq 0.$$

- Optimality criteria: (i) area under the curve;
  (ii) time to maximum concentration;
  and (iii) maximum concentration.

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- (c) Maximum concentration: $\eta(x_{max}, \theta) = g_3(\theta)$

- Use nominal values in Atkinson & Donev's (2004) text:
  $\theta_1^0 = 4.29, \theta_2^0 = 0.0589$ and $\theta_3^0 = 21.80$.

3.5 D_s-optimal Designs for the Quadratic Logistic Models)

In radiation research, we want to design in vivo multifraction experiments to estimate the $\alpha - \beta$ ratio (Taylor, Radiation Research, 1990).

$$p(x,\theta) = \frac{1}{1 + exp\{-a - b(x-m)^2\}} \qquad \theta^T = (a, b, m)$$

Using Elfving's theorem, Fornius and Nyquist, Communications in Statistics, 2010) used geometrical arguments and reported various D_s-optimal designs for estimating different subsets of θ.

3.6 Minimax Designs for Dose Response Studies

- Want to optimally design to, say minimize the maximal variance of the responses over the extrapolated doses.

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- Maximizing minimal efficiencies under several objectives in toxicological studies: Dette, Pepelyshev, Shpilev, Wong (Statistics and Its Interface, 2009), Bernoulli Journal (2009, 2010), Dette, Pepelyshev and Wong (Risk Analysis, 2011) and Dette, Pepelyshev and Wong (Journal of Pharmacokinetics and Pharmacodynamics, 2012)

3.6a Minimax Optimal Design: a definition

Suppose

$$y(x) = f^T(x)\theta + e(x)/\sqrt{\lambda(x)}, \quad x \in X$$

where $f^T(x)$ is a vector of known regression functions, $\lambda(x)$ is a known efficiency function and $e(x) \sim N(0, \sigma^2)$. If observations are independent, information matrix is proportional to

$$M(\xi) = \int_X \lambda(x) f(x) f^T(x) \xi(dx),$$

and the variance of the fitted response at x using ξ is proportional to

$$v(x, \xi) = var_\xi(f^T(x)\hat{\theta}) = f^T(x) M^{-1}(\xi) f(x).$$

Definition: ξ^* is minimax optimal design among all designs on X if

$$\xi^* = \arg\min_\xi \max_{x \in Z} v(x, \xi),$$

where Z is a user-selected compact set for prediction purposes.

3.6b Equivalence theorem for a Minimax-type criterion

Equivalence Theorem: ξ^* is minimax-optimal if and only if there exists a probability measure μ^* on $A(\xi^*)$ such that for all $x \in X$,

$$c(x, \mu^*, \xi^*) = \int_{A(\xi^*)} \lambda(x)(f^T(x)M(\xi)^{-1}f(a))^2 \mu^*(da) - v(a, \xi^*) \leq 0,$$

with equality at the support points of ξ^*. Here,

$$A(\xi) = \{a \in Z | v(a, \xi) = \max_{z \in Z} v(z, \xi)\}.$$

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- A proof is in Berger, King & Wong (Psychometrika, 2000), where they applied applied minimax optimal designs for item response models in education testing problems.
- μ^* can be shown to be a maximin probability measure
- Minimax efficiency lower bound can be directly found for any design using convex theory.

3.6c E-optimal designs for the Michaelis-Menten model on $X = [0, \tilde{x}]$ (Dette and Wong, Stat. & Prob. Letters, 1999)

The Michaelis-Menten model for a continuous response is

$$y = \frac{\theta_1 x}{\theta_2 + x} + \varepsilon, \;\; x > 0 \quad \theta^T = (\theta_1, \theta_2), \theta_1 > 0, \theta_2 > 0.$$

If ε is normally distributed with mean 0 and constant variance, the Fisher information matrix for a given design ξ is

$$M(\xi, \theta) = \int (\frac{\theta_1 x}{\theta_2 + x})^2 \begin{pmatrix} \frac{1}{\theta_1^2} & -\frac{1}{\theta_1(\theta_2+x)} \\ -\frac{1}{\theta_1(\theta_2+x)} & \frac{1}{(\theta_2+x)^2} \end{pmatrix} d\xi(x).$$

Let

$$w = \frac{\sqrt{2}(\theta_1/\theta_2)^2(1-\tilde{z})\{\sqrt{2}-(4-2\sqrt{2})\tilde{z}\}}{2+(\theta_1/\theta_2)^2\{\sqrt{2}-(4-2\sqrt{2})\tilde{z}\}^2}$$

and $\tilde{z} = \tilde{x}/(\theta_2 + \tilde{x})$. The locally E-optimal design has weight 1-w at $\tilde{x}$ and weight w at $\{(\sqrt{2}-1)\theta_2\tilde{x}\}/\{2-\sqrt{2})\tilde{x} + \theta_2\}$.

3.6d Table 1: Locally E-optimal designs for the Michaelis-Menten model on $X = [0, 200]$.

θ_1	θ_2	ξ_{PSO}		E-optimal designs	
100	150	46.52(0.693)	200(0.308)	45.51(0.693)	200(0.307)
100	100	38.15(0.677)	200(0.323)	38.15(0.677)	200(0.323)
100	50	24.78(0.617)	200(0.383)	24.78(0.617)	200(0.383)
100	10	6.52(0.260)	200(0.740)	6.52(0.260)	200(0.740)
100	1	0.70(0.022)	200(0.978)	0.70(0.022)	200(0.978)
10	150	46.50(0.707)	200(0.293)	46.50(0.707)	200(0.293)
10	100	38.14(0.707)	200(0.293)	38.14(0.707)	200(0.293)
10	50	24.78(0.706)	200(0.294)	24.78(0.706)	200(0.294)
10	10	6.52(0.684)	200(0.316)	6.52(0.684)	200(0.316)
10	1	0.70(0.188)	200(0.812)	0.70(0.188)	200(0.812)

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- discrepancy stubbornly remained and did not disappear
- simply calculation error from the formula; PSO gave right answer!

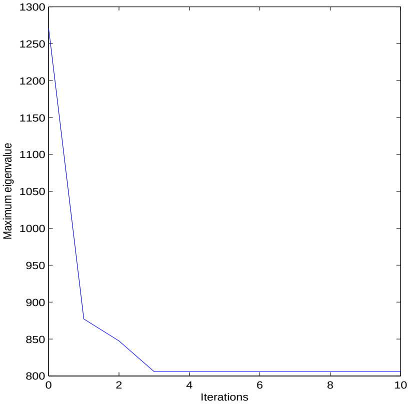
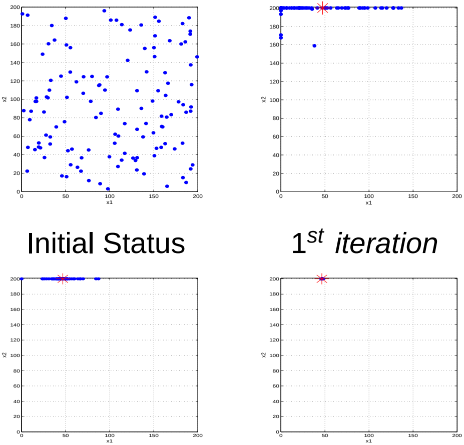


Figure 4: Plot of the maximum eigenvalue of $M(\xi, \theta)^{-1}$ versus the number of PSO iterations.



Initial Status | 1^{st} *iteration*

5^{th} *iteration* | 10^{th} *iteration*

Figure 5: The movement of particles in the PSO search for the E-optimal design for the Michaelis-Menten model at various stages. The red star in each of the three plots indicates the current best design.

3.6e Minimax Optimal Designs for Nonlinear Models

Assume there is a plausible region Θ for the unknown intercept (θ_1) and slope (θ_2) parameters in the two parameter logistic model, i.e.

$$(\theta_1, \theta_2) \in \Theta.$$

King & Wong (Biometrics, 2002) found minimax D-optimal designs when the form of Θ is a cartesian product.

For example, when $\Theta = [0, 3.5] \times [1, 3.5]$ and X is unrestricted:

x_i	-0.35	0.62	1.39	2.11	2.88	3.85
w_i	0.18	0.21	0.11	0.11	0.21	0.18

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w_i	0.18	0.21	0.11	0.11	0.21	0.18

- Algorithm for finding minimax optimal designs remains elusive.

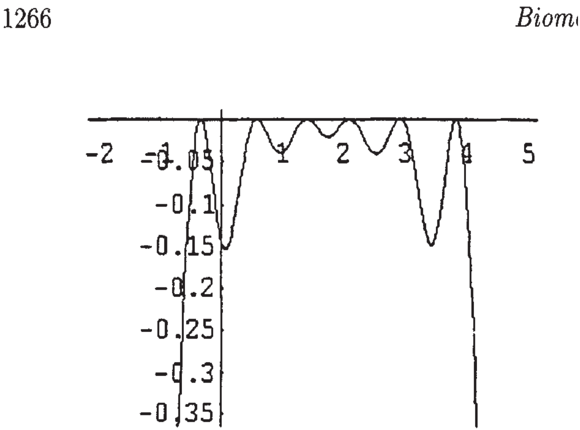

Figure 6: Plot of the directional derivative of claimed minimax D-optimal design for the logistic model.

Example 3.6f: A minimax D-optimal design for the logistic regression model when we have plausible ranges for the two parameters (King & Wong, Biometrics, 2000)

Consider the logistic model

$$p(x,\theta) = 1/\{1+\exp(-\theta_2(x-\theta_1))\}, \qquad \theta^T = (\theta_1, \theta_2).$$

The Fisher information matrix for ξ is $M(\xi,\theta)$ given by

$$\int \begin{pmatrix} \theta_2^2 p(x,\theta)(1-p(x,\theta)) & -\theta_2(x-\theta_1)p(x,\theta)(1-p(x,\theta)) \\ -\theta_2(x-\theta_1)p(x,\theta)(1-p(x,\theta)) & (x-\theta_1)^2 p(x,\theta)(1-p(x,\theta)) \end{pmatrix} d\xi(x$$

Goal: Find a minimax D-optimal design ξ^* such that

$$\xi^* = \arg\min_{\xi}\max_{\theta\in\Theta} \log(|M^{-1}(\xi,\theta)|).$$

Here Θ is a known set containing all plausible values of θ_1 and θ_2.

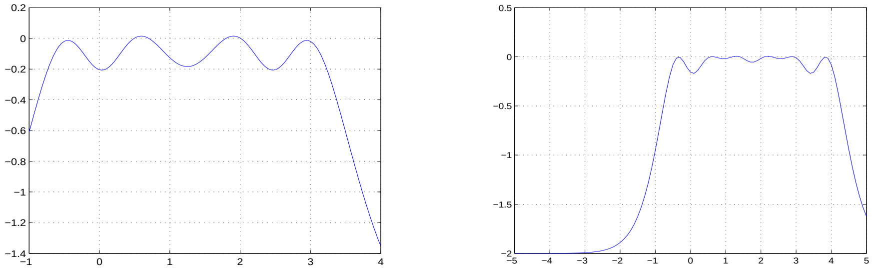

Figure 7: Plot of the directional derivatives $c(x, \xi_{PSO}, \mu^*)$ versus x for two cases:

(i) $\Theta = [0, 2.5] \times [1, 3.0]$ on $X = [-1, 4]$ (left)

(ii) $\Theta = [0, 3.5] \times [1, 3.5]$ on $X = [-5, 5]$ (right).

no. of particles for external(internal) optimization: 64(256) 32(512)
no. of iterations for external(internal) optimization: 100(200) 50(100)
Efficiency Lower Bounds of PSO-generated designs are both about 0.9924.

4 Discussion

Helpful to have a design website to find tailor-made optimal designs at

http://optimal-design.biostat.ucla.edu/optimal/

Illustrative examples in Berger & Wong, An Introduction to Optimal Designs for Social & Biomedical Research (John Wiley, 2009).

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- Implement PSO to find multiple-objective optimal designs; see Cook & Wong (JASA, 1994), Huang & Wong (Biometrics, 1998), Zhu & Wong (J. Biopharm. Stat., 2000), Imhof & Wong (Biometrics, 2000), Huang & Wong (Drug Information J., 2004)

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- Apply PSO to find optimal exact designs, minimum bias optimal designs and Bayesian Designs? What about optimal designs on a discrete design space? Models with correlated errors?

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- Apply PSO to find optimal exact designs, minimum bias optimal designs and Bayesian Designs? What about optimal designs on a discrete design space? Models with correlated errors?

- Expand website capabilities to find an optimal design for any model and any criterion (? - hopefully).

4.1 Other Nature-Inspired Algorithms

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- Artificial bee colony algorithm (2007)
- Monkey search (2008)

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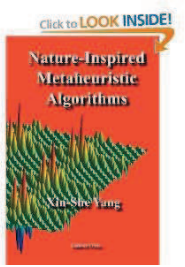
- Firefly algorithm (2009, 2010)
- Bat algorithm (2010)

4.2 Resources for Metaheuristic Optimization and Nature-Inspired Metaheuristic Codes

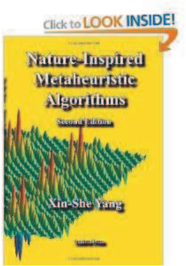
Scholarpedia, the peer-reviewed open-access encyclopedia:
http://www.scholarpedia.org/article/Metaheuristic_Optimization

Another is at
http://www.metaheuristic.com/metaheuristic_optimization.php

Xin-She Yang's 2008 book and updated in 2010:



2008



2010 (2^{nd} edition)

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- O'Brien (Journal of Data Science, 2005) noted that the locally D_s-optimal design for estimating θ_2 in the 2-compartmental model

$$\eta(x,\theta) = \frac{\theta_1}{\theta_1 - \theta_2}\{exp(-\theta_2 x) - exp(-\theta_1 x)\}$$

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- Huge memory space is needed especially for finding Bayesian optimal designs for nonlinear models (Duarte and Wong, 2012a)

4.4 Further Minimax Design Problems

(a) Power Logistic Model (Prentice, Biometrics, 1976):

$$p(x,\theta) = \frac{1}{\{1 + exp(\beta(x-\mu))\}^s}, \quad \theta \in \Theta = \{(\mu,\beta,s), \;\; \mu > 0 \;\; \& \;\; \beta > 0\}.$$

(b) Logistic Model with a nonlinear constraint on the parameter space:

$$log\,\frac{\pi(x)}{1-\pi(x)} = \beta(x-\mu), \quad \theta \in \Theta = \{(\mu,\beta), \;\; \mu > 0 \;\; \& \;\; \beta > 0\},$$

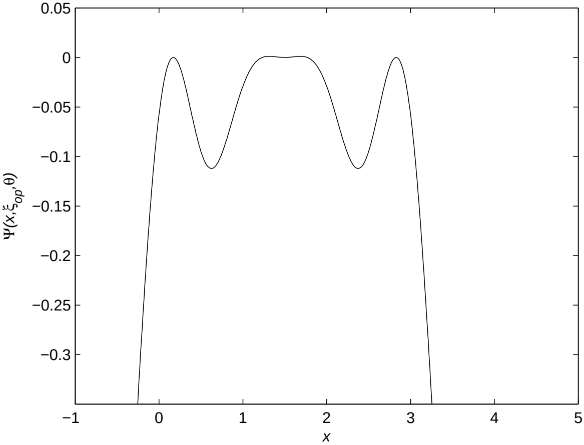
i.e. constrained space has a nonlinear relationship in μ and β.

Duarte and Wong (2012b) used SIP and found minimax D-optimal designs for such problems.

Table 2: Minimax D-optimal designs for the logistic model when the model parameters are functionally dependent inside the plausible region

	$[\mu^L, \mu^U]$	
	[0.5,1.0]	[0.5,2.5]
Constraint	ξ_{op}	ξ_{op}
$\beta \geq 2\ \mu$	-0.0680(0.5000)	0.2885(0.2796)
$\beta \in [0, 3]$	1.5680(0.5000)	1.2678(0.4408)
		2.7115(0.2796)
$\beta \leq 2\ \mu$	-0.2997(0.5000)	0.1710(0.2606)
$\beta \in [0, 3]$	1.7997(0.5000)	1.5000(0.4788)
		2.8290(0.2606)
$\beta \geq 2\ \mu^2$	-0.0680(0.5000)	0.2498(0.2772)
$\beta \in [0, 3]$	1.5680(0.5000)	1.2662(0.4457)
		2.7502(0.2772)
$\beta \leq 2\ \mu^2$	-0.6274(0.5000)	0.1710(0.2606)
$\beta \in [0, 3]$	2.1274(0.5000)	1.5000(0.4788)
		2.8290(0.2606)

Fig. 8: Plot of the directional derivative $\Psi(x, \xi_{op}, \theta)$ of the SIP-generated design ξ_{op} over X confirms that ξ_{op} is minimax D-optimal for the logistic model with $\beta \leq 2\mu^2$, $\mu \in [0.5, 2.5]$ and $\beta \in [0.0, 3.0]$



4.3 Tomlab

LATEST NEWS

Aug 23rd 2012
TOMLAB 7.9 released. Read more >>

Dec 16th 2011
TOMLAB 7.8 released. Read more >>

Jun 8th 2011
TOMLAB 7.7 released. New versions of CPLEX, GUROBI and KNITRO. Read more >>

Nov 24th 2010
TOMLAB 7.6 released. GUROBI now supports MIQP. Read more >>

Oct 1st 2010
TOMLAB 7.5 released. PROPT now supports binary and integer variables! Read more >>

Mar 24th 2010
TOMLAB 7.4 released. PROPT now has an automated scaling module. Read more >>

Dec 7th 2009
TOMLAB 7.3 released. GUROBI 2.0 released. Several Base Module updates! Read more >>

Aug 18th 2009
TOMLAB 7.2 released. New GUROBI solver now available. Read more >>

Aug 6th 2009
TOMLAB switches to BITROCK for multi-platform installation support. Read more >>

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TOMLAB v7.1 released. Many additional PROPT examples, MINLP support in KNITRO and more. Read more >>

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TOMLAB /CPLEX v12.2
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TOMLAB /CGO v7.8
Solver package for costly global optimization. The latest release of the solvers rbfSolve and EGO also handles integer variables. The package is best used in conjunction with TOMLAB /SOL or TOMLAB /OQNLP if integer variables are included.
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Klaus Schittkowski

4.4 Summary

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- Recall the NO FREE LUNCH THEOREM. For complex problems, need to hybridize algorithms!
- PSO methodology offers great promise and I believe represents a leap forward in the field of optimal experimental designs.
- Students should be more exposed to different types of optimization techniques - more interdisciplinary training!

Questions/Comments?

Please send them to Weng Kee Wong

(wkwong@ucla.edu)

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