Confidence Regions for the Location of Response Surface Optima: the R Package OptimaRegion

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Abstract

This papers describes methods implemented in the R package **OptimaRegion** for the computation of confidence regions on the location of the optima of response surface models. Both parametric (quadratic polynomial) and nonparametric (thin plate spline) models are supported. The confidence regions obtained do not rely on any distributional assumption, such as Normality of the response.

Keywords: Nonparametric regression, Response Surface Methodology, Optimization, Data-depth .

Introduction

The goal of many experiments in engineering and science is to find either the maximum, or "peak", or the minimum, or "deepest valley", of some response of interest. How to design and analyze optimization experiments are problems that pertain to the classical field of Response Surface Methodology (RSM) (Box and Draper 1987; del Castillo 2007). The classical approach for optimizing a response in RSM consists in optimizing a fitted model obtained from experimental data, treating it as if it were the true input/output description of the system under study, neglecting the inherent uncertainty of the fitted model. From a frequentist point of view, any property or characteristic of a response surface fitted from experimental data is subject to sampling variability, and hence it should be possible, in principle, to conduct statistical inference on them. Solutions to the problem of statistical inference in RSM have been proposed, usually assuming a polynomial response surface model fitted with ordinary least squares under a normality assumption (Myers and Montgomery 1995; del Castillo 2007). Even in such case, software to perform the computations is lacking. One of the most useful inferences in RSM is that of finding a confidence region (CR) on the location of the maximum or minimum of a response surface. These CRs have found several applications in engineering and science. For instance, (Carter, Wampler, Stablein, and Campbell 1982) proposed the idea of using a CR for the optimal dose combination of an anti-Cancer drug as a way to test for therapeutic synergism. If the CR for the optimal dose combination excludes all zero-dose treatment combinations, then there is statistically significant evidence that all of the components are therapeutically synergistic. Otherwise, there are components that can be eliminated from the formulation.

A CR on the optima can also be useful for finding a "design space" of a drug in pharmaceutical development (Peterson 2008). Brooks, Hunt, Blows, Smith, Bussiere, and Jennions (2005) use a CR on experimentally observed fitness responses to test whether an animal has achieved stabilizing selection as predicted by evolutionary biology. A CR on the optimal settings of a production process is useful in industrial experiments as their size provides a measure of robustness. They also provide a set of solutions within which the engineer can "tweak" the optimal recipe without jeopardizing the expected system response (del Castillo 2007).

Previous work on CRs for the location of response surface optima assume normal-distributed errors and a quadratic polynomial form (Peterson, Cahya, and del Castillo 2002; Cahya, del Castillo, and Peterson 2004). Early work on confidence regions (Box and Hunter 1954) focused on regions for stationary points of response surfaces, not necessarily on optimum points, and hence are of limited value (del Castillo and Cahya 2001). This paper shows methods implemented in the R package **OptimaRegion**, which allows users to find a CR on the location of the optima of both quadratic and thin plate spline models without recourse to normality. The CRs are data-depth based, and follow recent results on the computation of confidence regions of parametric functions.

Description of the problem

We wish to find a confidence region (CR) for the (global) optima of a function in k variables fitted from observed experimental data without relying in multivariate normality or any other distributional assumption of the data. We assume in this paper a maximization goal without loss of generality. In this paper, bootstrapping methods and their software implementation are presented that provide *valid* and *unbiased* confidence regions for the optima of a function fitted either using a linear regression (quadratic polynomial model) or a thin plate spline model. A **valid** $1-\alpha$ CR for a parameter θ, $\mathrm{CR}^{\theta}_{1-\alpha}$, is a set such that $P(\theta \in \mathrm{CR}^{\theta}_{1-\alpha}) \geq 1-\alpha$. Interest is of course in CR's that are smallest in size and still have confidence level of at least $1-\alpha$, and hence we will consider not only the coverage but the area of the CR's. Also, a $1-\alpha$ CR is **unbiased** if $P(\theta' \in \mathrm{CR}^{\theta}_{1-\alpha}) \leq 1-\alpha$ for all $\theta' \neq \theta$ (Casella and Berger 2002) (p. 446). That is, the probability of covering any wrong parameter should always be less than the probability of covering the true parameter.

More specifically, we wish to find a CR for the function:

$$\mathbf{x}^* \; = \; h(\mathbf{x}; \hat{\boldsymbol{\beta}}) \; = \; \arg\max f(\mathbf{x}, \hat{\boldsymbol{\beta}})$$

where $f(\mathbf{x}, \hat{\boldsymbol{\beta}})$ is *either* a quadratic polynomial regression model in $\mathbf{x}$ *or* a Thin Plate Spline model in $\mathbf{x}$. In both cases, we assume maximization without loss of generality. In the quadratic polynomial model, $\mathbf{x}^* \in \mathbb{R}^k$ is a random vector with a sampling distribution that depends on the sampling distribution of the $p \times 1$ least squares estimator $\hat{\boldsymbol{\beta}}$ in $\boldsymbol{Y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$ where $\boldsymbol{X}$ is a $n \times p$ design matrix with columns corresponding to the terms in the quadratic polynomial model $f(\mathbf{x}, \hat{\boldsymbol{\beta}})$, and the random errors ε_i in $\boldsymbol{\varepsilon}$ are to be i.i.d. with zero mean, constant variance and with an unknown and unspecified distribution. (Woutersen and Ham 2013) have recently studied the asymptotic coverage properties of bootstrap regions for any parametric function $h(\mathbf{x}; \hat{\boldsymbol{\beta}})$. We use and operationalize their results for the case $h(\mathbf{x}; \hat{\boldsymbol{\beta}}) = \arg\max f(\mathbf{x}, \hat{\boldsymbol{\beta}})$, where the output is in $\mathbb{R}^k$.

Naive bootstrapping approach

A direct application of the idea of bootstrapping, referred as the "AD" bootstrap method in (Woutersen and Ham 2013) consists in fitting many response surface models, optimizing each and trimming the outmost α percent $\mathbf{x}^* = h(\boldsymbol{\beta})$ vectors using some method that orders interior and exterior multivariate data. Unfortunately (see table 1 below), this method does not provide valid confidence regions, i.e., their coverage is smaller than the advertised coverage. The reason is that by trimming the $h(\boldsymbol{\beta})$ values we are eliminating extreme observations of h that occurred because either a) $\boldsymbol{\beta}$ was very extreme or b) because $\boldsymbol{\beta}$ is not very extreme but $h(\boldsymbol{\beta})$ is extreme. A CR on $h(\boldsymbol{\beta})$ should exclude instances where h, and not $\boldsymbol{\beta}$, are extreme. This is achieved with the method implemented in the **OptimaRegion** package, but not with this naive approach.

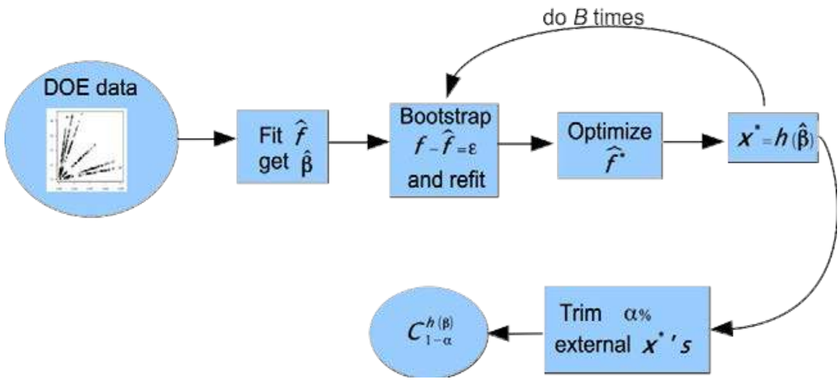

Figure 1: A naive bootstrapping approach to compute the CR of the optima of a response surface.

Implementation of the bootstrapping methods in OptimaRegion

Woutersen and Ham (Woutersen and Ham 2013) propose the "CS" (confidence set) bootstrap method for finding confidence regions of functions of parameters. The method is based on the following steps:

1 obtain a $100(1-\alpha)\%$ CR for $\boldsymbol{\beta}$ from the asymptotic distribution of $\hat{\boldsymbol{\beta}}$.

2 For each $\boldsymbol{\beta} \in \mathrm{CR}_{1-\alpha}^{\boldsymbol{\beta}}$, evaluate $h(\boldsymbol{\beta})$.

3 Let $\mathrm{CR}_{1-\alpha}^{h(\boldsymbol{\beta})} = \{\tau \in \mathbb{R}^k | \tau = h(\boldsymbol{\beta}) \text{ for all } \boldsymbol{\beta} \in \mathrm{CR}_{1-\alpha}^{\boldsymbol{\beta}}\}$

To estimate this confidence region, these authors propose bootstrapping in steps 1 and 3:

$\mathbf{1_B}$ Obtain an estimate of the $100(1-\alpha)\%$ CR for $\boldsymbol{\beta}$ by bootstrapping B instances of $\hat{\boldsymbol{\beta}}$. These instances make $\widehat{\mathrm{CR}}_{1-\alpha}^{\boldsymbol{\beta}}$;

$\mathbf{2_B}$ For each $\boldsymbol{\beta} \in \widehat{\mathrm{CR}}_{1-\alpha}^{\boldsymbol{\beta}}$, evaluate $h(\boldsymbol{\beta})$.

$\mathbf{3_B}$ Let $\widehat{\mathrm{CR}}_{1-\alpha}^{h(\boldsymbol{\beta})} = \{\tau \in \mathbb{R}^k | \tau = h(\boldsymbol{\beta}) \text{ for all } \boldsymbol{\beta} \in \widehat{\mathrm{CR}}_{1-\alpha}^{\boldsymbol{\beta}}\}$

Note that in order to implement this method for $h(\mathbf{x}; \hat{\boldsymbol{\beta}}) = \arg\max f(\mathbf{x}, \hat{\boldsymbol{\beta}})$, *we need a means to define the "innermost"* $\boldsymbol{\beta}$ *parameters in step* $\mathbf{1_B}$*, and an optimization method that finds the global maximums of each* $h(\boldsymbol{\beta})$ *in step* $\mathbf{2_B}$. **OptimaRegion** uses the notion of data depth (as implemented in the **DepthProc** package) in step $\mathbf{1_B}$ and nonlinear programming methods with multiple restarts as implemented in the **nloptr** package in step $\mathbf{2_B}$. See the appendix for a brief description of data depth methods. In **OptimaRegion** we use Tukey's data depth (see Appendix) to order the B instances $\widehat{\boldsymbol{\beta}}$ and trim the α % outermost (the α % with lowest D_T value; for instance, points such that $D_T(\mathbf{x}) = 0$ define the convex hull of F). This yields $\widehat{\mathrm{CR}}_{1-\alpha}^{\boldsymbol{\beta}}$ in step $\mathbf{1_B}$. Furthermore, since we are computing $\widehat{\mathrm{CR}}_{1-\alpha}^{\boldsymbol{\beta}}$ pointwise for a finite number of B vectors $\boldsymbol{\beta}$, our final confidence region for $h(\boldsymbol{\beta})$ will also be a pointwise region. This means that to end up with a *region* we need some additional rule that defines the boundary of the region. In (Woutersen and Ham 2013) the authors propose to use an arbitrary quantity $\eta > 0$ and define the CR for $h(\boldsymbol{\beta})$ to be the set of all $\boldsymbol{\beta}$ that are no farther than the euclidean distance η from each of the B $h(\boldsymbol{\beta})$ values (in $\mathbb{R}^2$ the CR will then be composed of the union of B circles around each $\mathbf{x}^*$). While this step was specified in order to be able to proof the validity of the resulting CR, in practice it

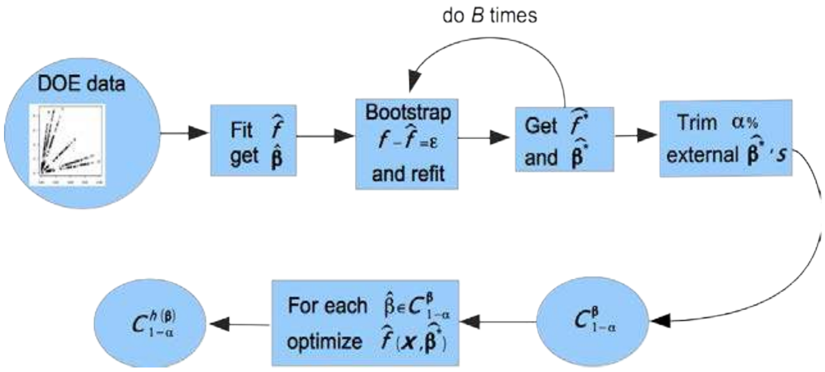

Figure 2: Overview of the bootstrapping approach implemented in **OptimaRegion**, following the "CS" method in (Woutersen and Ham 2013)

is not clear how to select the radius η to make the resulting CR as small as possible and avoid grossly conservative CR's. The PDF files created by the functions in **OptimaRegion** display the CRs by plotting the convex hull of all the points generated. The coordinates of all the generated points inside the CR are also returned.

In what follows we concentrate in computational methods for obtaining CR's for $h(\mathbf{x}; \hat{\boldsymbol{\beta}}) = \arg\max f(\mathbf{x}, \hat{\boldsymbol{\beta}})$ for the particular case $k = 2$. The underlying global optimization process of a non-convex function makes finding the desired confidence regions a very difficult problem for $k > 2$. Therefore, **OptimaRegion** is currently limited to problems with 2 controllable factors.

Functions in package OptimaRegion

There are 3 main functions in the **OptimaRegion** package:

Function	Objective
`OptRegionQuad`	Computes distribution-free bootstrapped confidence regions for the location of the optima of a quadratic polynomial model in 2 regressors
`OptRegionTps`	Computes distribution-free bootstrapped confidence regions for the location of the optima of a Thin Plate Spline model in 2 regressors
`CRcompare`	Computes bootstrapped confidence intervals for the distance between the optima of two different response surface models, either quadratic polynomials or thin plate spline models

Examples

Example 1. CR on the maximum of a fitted quadratic polynomial using `OptRegionQuad`.- Consider a mixture-amount experiment in two components (Drug dataset) where the effectiveness of the drug (a percentage) is the response, which in many cases has value zero. Hence, the data cannot be considered normal and classic approaches to find a CR cannot be used. Thus, we try using `OptRegionQuad` as it does not rely on any normality assumption. Given the shape of the experimental region, the `triangularRegion` switch is set to on, with upper and right vertices as specified for `vertex1` and `vertex2` (the other vertex is the origin). This indicates the limits of the experimental region, and therefore, the region where the maxima should be seek. The R command is:

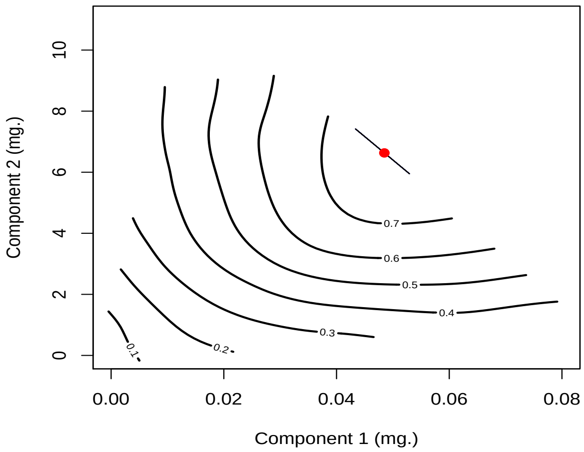

Figure 3: Example 1: a 95% CR on the maximum of a 2-drug mixture amount experiment, `Drugs` datafile. PDF file generated with the `OptRegionQuad` function.

```
out <- OptRegionQuad(X = Drug[,1:2], y = Drug[3], nosim = 500, LB = c(0,0),
UB = c(0.08,11), xlab = "Component 1 (mg.)", ylab = "Component 2 (mg.)",
triangularRegion = TRUE, vertex1 = c(0.02,11), vertex2 = c(0.08,1.8),
outputPDFFile = "Mixture_plot.pdf")
```

The resulting 95% confidence region generated in the PDF file is shown in Figure 3, which also shows smoothed contours of the response. Note this are *not* the quadratic polynomial contours. Also, note how the CR is "pushed" against the constraint and results in a "thin line". The red dot is the centroid of all the generated maxima, it constitutes a "bagging" point estimate of $\mathbf{x}^*$.

Example 2. CR on the global maximum of a fitted Thin Plate Spline model for a mixture-amount experiment using `OptRegionTps`.- Consider next the same mixture-amount experiments as before (`drugs` dataset) but suppose we think the quadratic polynomial model provides is not flexible enough to represent the true surface. Instead, we can try fitting and optimizing a Thin Plate Spline (TPS) model using function `OptRegionTps`.

```
out <- OptRegionTps(X = Drug[,1:2], y = Drug[,3], nosim = 500, lambda = 0.05,
LB = c(0,0), UB = c(0.08,11), xlab = "Component 1 (mg.)", ylab = "Component 2 (mg.)",
triangularRegion = TRUE, vertex1 = c(0.02,11), vertex2 = c(0.08,1.8),
outputPDFFile = "Mixture_plot.pdf")
```

In contrast with example 1, `OptRegionTps` will take a few minutes to complete the computations in a fast PC. Note the parameter `lambda=0.05`; this is the penalization parameter when fitting a TPS model. Larger values of `lambda` make the fitted model less "wiggly". The confidence levels obtained are conditional on the pre-selected value of `lambda`. The PDF output file showing the CR is shown in Figure 4.

The CR contains area in the interior of the triangular experimental region. The linear boundaries of the shaded CR are the result of using the convex hull of the optima generated by the bootstrapping algorithm. Increasing the number of bootstraps may smooth the boundaries somewhat (i.e., shorter linear segments) but the computation time will increase accordingly. Despite being a better model for this dataset, the more flexible character of the TPS model contains a good deal

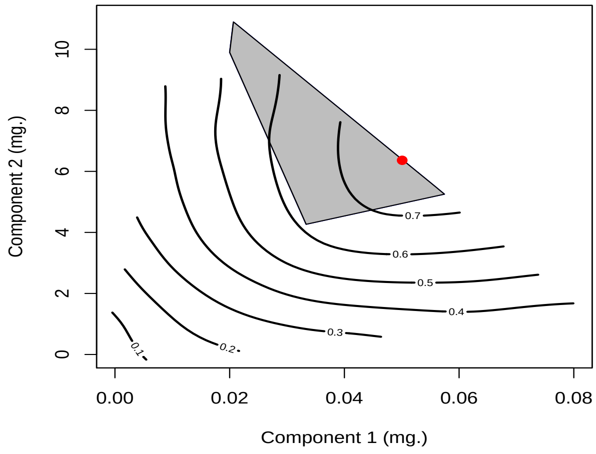

Figure 4: Example 2: a 95% CR on the maximum of a 2-drug mixture amount experiment, `Drugs` datafile. PDF file generated with the `OptRegionTps` function.

of uncertainty about the location of the maximum drug components that maximizes the efficacy.

Example 3. CR on the global maximum of a fitted Thin Plate Spline model for a factorial experiment using `OptRegionTps`.- We now illustrate the use of the `OptRegionTps` function for and experiment where the factors are centered around zero and the experimental region is a square. Suppose we generate some dummy 'X' and 'y' data randomly:

```
X <- cbind(runif(100,-2,2), runif(100,-2,2))

y <- as.matrix(72 - 11.78*X[,1] + 0.74*X[,2] - 7.25*X[,1]^2 - 7.55*X[,2]^2 -
  4.85*X[,1]*X[,2] + rnorm(100,0,8))
```

Next we compute a 95% CR on the maxima of a fitted TPS model:

```
out <- OptRegionTps(X = X, y = y, nosim = 200, LB = c(-2,-2), UB = c(2,2),
  xlab = "X1", ylab = "X2")
```

Note we did not specify a triangular region. The PDF file created on completion is shown in Figure 5 and displays the corresponding region, together with the contours of the fitted TPS model.

Example 4. Computing confidence *intervals* on the distance between two response surfaces.- Suppose we have experimental data from which we can fit a quadratic polynomial model to each of two different responses. We now wish to investigate if the "peaks" of each response are significantly close. A confidence interval on the distance between the two maxima can be computing with the `CRcompare` function. To use this function, we need to provide the 'X' and 'y' experimental data for each response. Let's create some dummy (random) data for illustration purposes:

```
X1 <- cbind(runif(100,-2,2), runif(100,-2,2))

y1 <- as.matrix(72 - 11.78*X1[,1] + 0.74*X1[,2] - 7.25*X1[,1]^2 - 7.55*X1[,2]^2 -
    4.85*X1[,1]*X1[,2] + rnorm(100,0,8))
```

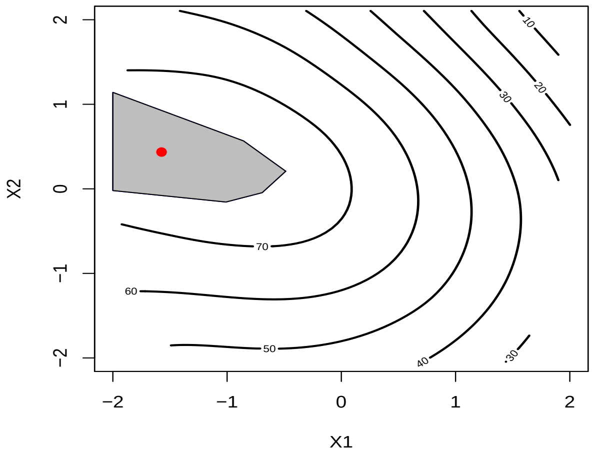

Figure 5: Example 2: a 95% CR on the maximum of a 2 factor randomly generated factorial experiment over a squared region. PDF file generated with the `OptRegionTps` function.

```
X2 <- cbind(runif(100,-2,2), runif(100,-2,2))

y2 <- as.matrix(72 - 11.78*X2[,1] + 0.74*X2[,2] - 7.25*X2[,1]^2 - 7.55*X2[,2]^2 -
    4.85*X2[,1]*X2[,2] + rnorm(100,0,8))
```

We next run the `CRcompare` routine with this input-output data:

```
out <- CRcompare(X1 = X1, y1 = y1, X2 = X2, y2 = y2, responseType = 'Quad',
   nosim1and2 = 200, alpha = 0.05, LB1 = c(-2,-2), UB1 = c(2,2), LB2 = c(-2,-2),
   UB2 = c(2,2) )
```

Note we specified a quadratic ('Quad') response model for both responses and 200 bootstrap iterations. Also note that the lower and upper bounds within which each response may have its maximum can differ ('maximization' is TRUE by default). `CRcompare` will run either `OptRegionQuad` or `OptRegionTps` for each response and compute all the pairwise distances from the two CR's. It will then bootstrap the distances and will output the corresponding bootstrap confidence interval on the mean and median distance:

```
> out$mean
[1] 0.3643884

> out$median
[1] 0.305715

> out$ciMean
     conf
[1,] 0.95 36.43 984.66 0.3324372 0.406087

> out$ciMedian
     conf
[1,] 0.95 18 966.76 0.2833316 0.3490922
```

Hence, a 95% confidence interval on the mean distance is (0.3324,0.4060) and a 95% confidence interval on the median distance is (0.2833,0.3490).

Numerical evaluation of coverage probability

For a given point $\mathbf{x}$ (equal to $\mathbf{x}^*$ or any other point), the coverage is defined as the proportion of times $\mathbf{x} \in \widehat{\mathrm{CR}}^{\boldsymbol{\beta}}_{\mathbf{1}-\alpha}$ in N_s trials from simulated data.

Wei and Lee (Wei and Lee 2012) show how a data-depth confidence region is second order accurate, that is, its coverage error (the difference between the actual coverage and the nominal confidence level) is of order n^{-1} where n denotes the sample size. They showed this result holds for different depth measures, including Tukey's data depth measure. Here we evaluate the performance of the functions `OptRegionQuad` and `OptRegionTps` in **OptimaRegion** via Monte Carlo simulation.

Quadratic polynomial model.

A CR for the optima of a quadratic polynomial model using the method described above is obtained using the `OptRegionQuad` function. Table 1 shows some coverage levels for the true maximum of the simulated response surface $f(\mathbf{x})$ compared with the naive bootstrapping approach referred earlier. Here

$$f(\mathbf{x}) = 90.79 - 1.095x_1 - 1.045x_2 - 0.775x_1x_2 - 2.781x_1^2 - 2.524x_2^2$$

to which i.i.d. $N(0, \sigma^2)$ noise was added. This function has a single maximum at $\mathbf{x}^* = (-0.1716, -0.1806)'$. The points $\mathbf{x}$ at which the function was simulated were the 11 runs in a rotatable Central Composite Design with a domain of radius $\sqrt{2}$ around the origin (Box and Draper 1987; del Castillo 2007) with 11 runs, in addition to sets of 11 runs randomly generated according to a uniform distribution on the square that goes from $(-\sqrt{2}, -\sqrt{2})$ in its lower left corner to $(\sqrt{2}, \sqrt{2})$ in the upper right corner, giving a total of n observations.

The results on Table 1 show how, compared with the naive bootstrapping approach, only the approach implemented in the `OptRegionQuad` function generates valid confidence regions, although always achieving higher than advertised coverages[1]. A reason for this behavior is that the final CR contour is obtained from the convex hull of the optima $\mathbf{x}^*$ which will tend to provide conservative coverage regardless of n and σ (see Table 2). The naive bootstrap method, in contrast, does not achieve the nominal coverage and cannot be recommended.

However, the areas of the CRs computed by `OptRegionQuad` are quite small, rapidly decreasing in size as n increases (Table 2), a very desirable property. Finally, Table 3 shows that the CRs obtained by `OptRegionQuad` are *unbiased*, since the coverage of non-optimal points is always lower than $1 - \alpha$, with lower coverages the farther is the non-optimal point from $\mathbf{x}^*$.

Thin Plate Spline model.

For the Thin-Plate Spline coverage analysis, the true simulated function was:

$$f(x_1, x_2) = \left((x_1 - 2)^2 + (x_2 - 2)^2 - (x_1 - 2) + 2(x_1 - 2)(x_2 - 2)\right) \exp(-(x_1 - 2)^2 - (x_2 - 2)^2)$$

defined in the region $R = \{0 \leq x_1 \leq 5, 0 \leq x_2 \leq 5\}$, which has a global maximum in this region[2] at $(x_1^*, x_2^*) = (1.2542, 1.4634)$. Figure 6 shows how this surface looks like. In each Monte

[1]Recall that the estimated standard error of the estimated coverage $\hat{p}$ is given by $\sqrt{\hat{p}(1 - \hat{p})/n}$, so all the estimated coverages presented in this paper are very precise.

[2]Note it has another local maxima and a deep minimum as well within the region of interest.

Table 1: Estimated coverages of bootstrapped $(1-\alpha)100\%$ CRs for the maximum of a quadratic polynomial regression model. N_s is the number of simulations, B is the number of bootstrapped samples, n is the sample size. Simulated noise has $\sigma = 2$.

CR type	N_s	B	α	n (reps.)	coverage
Naive	1000	1000	0.10	55 (5)	0.843
Naive	1000	1000	0.10	1100 (100)	0.868
`OptRegionQuad`	1000	1000	0.05	1100 (100)	0.981
`OptRegionQuad`	1000	1000	0.10	1100 (100)	0.979
`OptRegionQuad`	1000	1000	0.20	1100 (100)	0.930

Table 2: Estimated coverages of the **optimal point** of a 95% bootstrapped CR as obtained by `OptRegionQuad` for the maximum of a quadratic polynomial regression model. In all cases, $N_s = 1000$, and $B = 1000$ were used. Maximum area in the search region is $8 = (-\sqrt{2}, \sqrt{2}) \times (-\sqrt{2}, \sqrt{2})$.

$n(reps.)$	coverage	σ	$\overline{\text{area}}$	sd.(area)	$\frac{\overline{\text{area}}}{\text{max area}}$	$\frac{\text{sd(area)}}{\text{max area}}$
1100(100)	0.981	2	0.007	0.00087	0.00088	0.0001
2200(200)	0.978	2	0.0036	0.00036	0.00045	0.000045
5500(500)	0.987	2	0.0014	0.00013	0.00018	0.000016
1100(100)	0.988	5	0.052	0.012	0.0065	0.0015
2200(200)	0.984	5	0.023	0.0037	0.0029	0.00046
5500(500)	0.985	5	0.009	0.0011	0.0012	0.00014
1100(100)	0.983	10	0.475	0.4004	0.059	0.0501
2200(200)	0.981	10	0.137	0.068	0.0172	0.0085
5500(500)	0.987	10	0.041	0.0083	0.0052	0.00104

Carlo simulation we generate n uniformly distributed random $\mathbf{x}$ values over R with observations $f(\mathbf{x}) + \epsilon$ where $\epsilon \sim N(0, \sigma^2)$ are i.i.d.

Computing a CS-Bootstrap confidence region for a Thin Plate Spline (TPS) model provides higher than advertised coverages of the optimum point, almost always close to 100 %, but with sizes (areas) that decrease rapidly as more experiments are performed (Table 4). These results were obtained with the `OptRegionTps.R` code.

As it can be seen in Table 5, the coverage percentage of *non-optimal* points is less than the confidence level $1-\alpha$, with coverage that decays as we consider non-optimum points farther than the optimum (x_1^*, x_2^*). This indicates the CS-bootstrapped confidence regions obtained by `OptRegionTps` are also unbiased.

Appendix. Data depth measures

A data depth is a measure of the centrality of a point with respect to the rest of the data, a notion particularly useful in a multivariate setting since it helps to order the data. Given a set of points $F = \{\mathbf{x_1}, \mathbf{x_2}, ...\mathbf{x_n}\}$, $\mathbf{x_i} \in \mathbb{R}^\mathbf{k}$, a data depth measure associated with an additional point $\mathbf{x}$ is a real-valued function $d(\mathbf{x}|F)$. In what follows we omit the dependency on the rest of the dataset. Different data depth measures have been proposed based on some commonly accepted properties (e.g., (Liu 1990)):

- Affine invariance: $d(\mathbf{x}) = d(\mathbf{A}\mathbf{x} + \mathbf{b})$ holds for any non-singular matrix $\mathbf{A}$ and any vector $\mathbf{b}$, i.e., the depth measure is invariant to rigid transformations

Table 3: Estimated coverages of **non-optimal** points $(a \cdot x_1^*, b \cdot x_2^*)$ using 95% bootstrapped CRs as obtained by `OptRegionQuad` for the maximum of a quadratic polynomial regression model. In all cases, $n(reps.) = 5500(500)$, $N_s = 1000$, and $B = 1000$. The last case ($a = b = 1$) corresponds to the coverage of the true optimum point.

coverage	σ	a	b
0.760	5	1.20	1.00
0.047	5	1.50	1.00
0.008	5	0.50	1.00
0.000	5	0.20	1.00
0.000	5	2.00	1.00
0.795	5	1.00	1.20
0.083	5	1.00	1.50
0.001	5	1.00	0.50
0.000	5	1.00	0.20
0.000	5	1.00	2.00
0.985	**5**	**1.00**	**1.00**

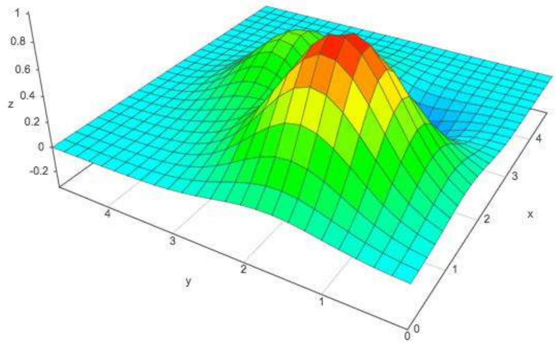

Figure 6: True response surface used in the `OptRegionTps` coverage simulation experiments.

- Maximality at the center: $d(\mathbf{x})$ achieves its maximum at the center $\mathbf{x_c}$ of the dataset. Here the notion of "center" needs to be defined.
- Monotonicity: the depth of a point deceases monotonically as it moves away from $\mathbf{x_c}$
- Vanishing at infinity: $d(\mathbf{x} - \mathbf{x_c}) \to \mathbf{0}$ as $||\mathbf{x} - \mathbf{x_c}|| \to \infty$.

Among the many data depth notions, a particularly intuitive definition which meets the conditions above, and perhaps the most used in practice, is Tukey's data depth measure (Tukey 1975), sometimes called the half space depth. It is defined as:

$$D_T(\mathbf{x}, F) = \min_{||\mathbf{u}||=\mathbf{1}} \text{card}\{\mathbf{u'x_i} \leq \mathbf{u'x}\}$$

where the minimization is over all k-dimensional vectors $\mathbf{u}$ of unit norm. The depth of point $\mathbf{x}$ is therefore equal to the smallest number of points in the dataset that can be found in any closed half space with a boundary that passes through point $\mathbf{x}$. This involves a computational problem in practice. Practically all of the Tukey depth functions available today in statistical software use an algorithm due to (Struyf and Rousseeuw 34) which has a time complexity $O(sk^3 + skn)$ where s random directions are generated through point $\mathbf{x}$, n is the number of points in the dataset and

Table 4: Estimated coverages of the **optimal point** of 95% bootstrapped CRs as obtained by `OptRegionTPS` for the global maximum of a Thin Plate Spline model. In all cases, $N_s = 500$, $B = 200$, $\lambda = 0.04$, and $\sigma = 0.5$ were used. Maximum area in the search region is $25 = (0,5) \times (0,5)$.

n	coverage	$\overline{\text{area}}$	sd.(area)	$\frac{\overline{\text{area}}}{\text{max area}}$	$\frac{\text{sd(area)}}{\text{max area}}$
100	0.988	12.92	6.00	51.68	24.01
150	0.998	11.76	4.75	47.04	19.00
200	1.000	7.14	2.89	28.56	11.56
250	1.000	6.35	2.42	25.40	9.68
300	0.992	5.25	2.26	21.02	9.05
500	0.998	3.90	1.59	15.61	6.36

Table 5: Estimated coverages of **non-optimal** points $(a \cdot x_1^*, b \cdot x_2^*)$ using 95% bootstrapped CRs as obtained by `OptRegionTps` for the maximum of a Thin Plate Spline model. In all cases, $n = 300$, $N_s = 500$, $B = 200$, $\lambda = 0.04$, and $\sigma = 0.5$. The last case ($a = b = 1$) corresponds to the coverage of the true optimum point.

coverage	a	b
0.860	1.20	1.00
0.950	0.20	1.00
0.780	1.40	1.00
0.518	0.00	1.00
0.922	1.00	1.37
0.914	1.00	0.68
0.690	1.00	0.34
0.554	1.00	1.71
0.992	**1.00**	**1.00**

k is the dimensionality of the data. Future versions of **OptimaRegion** will include choices for other depth measures.

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