In this supplementary material, the region-design repair (RDR) and design-region repair
(DRR) approaches are illustrated for a constrained experimental design problem involving three
non-mixture variables. The original constrained experimental region (CER) is a cube specified
by the single-variable constraints (SVCs)

\[ \begin{align*}
1 & \leq x_1 \leq 5 \\
3 & \leq x_2 \leq 7 \\
2 & \leq x_3 \leq 6
\end{align*} \]  

(S.1)

The original design is a face-centered cube including a center point, with the 15 points listed in
columns A, B, and C as marked in column E of Table S.1. Suppose the experimental design was
performed, and it was discovered that the points in rows 1 and 5 of Table S.1 were unacceptable.
Note that both of these points have \( x_1 \) and \( x_2 \) at their lower limits, indicating that both of these
variables cannot be at their lower limits simultaneously.

S.1 RDR Example

We now illustrate the RDR approach described in Section 2 to repair the 15-point original
design and CER for this example. In the first step of the RDR approach, the CER must be
repaired. Suppose that a subject-matter expert developed the multiple-variable constraint (MVC)

\[ 4x_1 + 4x_2 - x_3 \geq 18 \]  

(S.2)

to eliminate the two unacceptable design points and nearby points in the CER that would be
unacceptable. Hence, the CER repaired using the RDR approach is specified by the constraints in
Equations (S.1) and (S.2).
TABLE S.1. Variable Settings for the 15 Points in the Original Experimental Design, RDR and DRR Designs, and New Designs for the RDR and DRR Regions for a Simple Example Involving Three Non-Mixture Variables

| Point # | $x_1$ | $x_2$ | $x_3$ | Point Type\(^{(a)}\) | Original Design | RDR Design, D-opt. | New D-opt. Design, RDR Region | DRR Design | New D-opt. Design, DRR Region |
|---------|-------|-------|-------|-----------------------|-----------------|---------------------|-----------------------------|-------------|-------------------------------|
| 1       | 1     | 3     | 2     | OV                    |                 |                     | X\(^{(b)}\)               |             |                               |
| 2       | 5     | 3     | 2     | OV                    | X               |                     | X                          | X           | X                             |
| 3       | 1     | 7     | 2     | OV                    | X               |                     | X                          | X           | X                             |
| 4       | 5     | 7     | 2     | OV                    | X               |                     | X                          | X           | X                             |
| 5       | 1     | 3     | 6     | OV                    |                 |                     | X\(^{(b)}\)               |             |                               |
| 6       | 5     | 3     | 6     | OV                    | X               |                     | X                          | X           | X                             |
| 7       | 1     | 7     | 6     | OV                    | X               |                     | X                          | X           | X                             |
| 8       | 5     | 7     | 6     | OV                    | X               |                     | X                          | X           | X                             |
| 9       | 3     | 5     | 2     | OCPC                  | X               |                     | X                          |             |                               |
| 10      | 3     | 5     | 6     | OCPC                  | X               |                     | X                          |             |                               |
| 11      | 3     | 3     | 4     | OCPC                  | X               |                     | X                          |             |                               |
| 12      | 3     | 7     | 4     | OCPC                  | X               |                     | X                          | X           | X                             |
| 13      | 1     | 5     | 4     | OCPC                  | X               |                     | X                          |             |                               |
| 14      | 5     | 5     | 4     | OCPC                  | X               |                     | X                          | X           | X                             |
| 15      | 3     | 5     | 4     | OC                    | X               |                     | X                          |             |                               |
| 16      | 2     | 3     | 2     | RDRV                  | X               |                     | X                          |             |                               |
| 17      | 1     | 5     | 6     | RDRV                  | X               |                     | X                          |             |                               |
| 18      | 1     | 4     | 2     | RDRV                  | X               |                     | X                          |             |                               |
| 19      | 1.75  | 3.75  | 4     | RDR CPC               |                 |                     | X                          |             |                               |
| 20      | 2.8   | 4.8   | 2     | RDR CPC               |                 |                     | X                          |             |                               |
| 21      | 2.9   | 4.9   | 4     | RDBC                  |                 |                     | X                          |             |                               |
| 22      | 3     | 3     | 6     | RDRRV                 |                 |                     | X                          |             |                               |
| 23      | 1.6   | 3.6   | 2.6   | DRRSP1                |                 |                     | X                          |             |                               |
| 24      | 1.9   | 3.9   | 5.1   | DRRSP5                |                 |                     | X                          |             |                               |
| 25      | 1     | 4.8   | 2     | DRRV                  |                 |                     | X                          |             |                               |
| 26      | 1     | 5.7   | 6     | DRRV                  |                 |                     | X                          |             |                               |
| 27      | 1.25  | 3     | 3.55  | DRRV                  |                 |                     | X                          |             |                               |
| 28      | 2.8   | 3     | 2     | DRRV                  |                 |                     | X                          |             |                               |
| 29      | 2.8864| 4.8636| 3.9590| DRRC                 |                 |                     | X                          |             |                               |
| 30      | 3.14  | 5.14  | 6     | DRR CPC               |                 |                     | X                          |             |                               |
| 31      | 3.7   | 3     | 6     | DRRV                  |                 |                     | X                          |             |                               |

\(^{(a)}\) OV = original vertex, OCPC = original constraint plane center, OC = original center, RDRV = RDR vertex, RDR CPC = RDR constraint plane center, RDRC = RDR center, DRR SP1 = DRR shrunken point 1, DRR SP5 = DRR shrunken point 5, DRRV = DRR vertex, DRR C = DRR constraint center, DRR CPC = DRR constraint plane center.
\(^{(b)}\) Denotes an original design point that was found to be unacceptable.

For the second step of the RDR approach, Design-Expert (Stat-Ease 2017) was used to D-optimally augment the 13 acceptable original design points with two replacement points chosen from the set of vertices and face centroids of the repaired CER. A point-exchange algorithm was used assuming a quadratic model in the three non-mixture variables. The RDR experimental design points are listed in columns A, B, and C, as marked in column F of Table S.1. The two replacement design points are listed in rows 16 and 17 of Table S.1. Note that these replacement
points are new vertices of the repaired CER near each of the corresponding unacceptable design points (which were vertices of the original CER).

The 15-point RDR experimental design was evaluated using the approach discussed in Section 4. A new 15-point design was generated using Design-Expert (Stat-Ease 2017) consisting of the center point and a subset of the vertices and constraint-plane center points of the RDR CER selected using a point-exchange algorithm. This design structure is analogous to that of the original design, except that the repaired CER is polyhedral whereas the original CER is cuboidal. A D-optimal approach assuming a quadratic model in the three variables was used. The 15 points in the resulting new design for the RDR CER are listed in columns A, B, and C as marked in column G of Table S.1. The values of the relative efficiencies [given in Equations (11) and (12)] of the RDR design compared to the new design for the RDR CER are $D\text{-Eff}_{\text{Rel}} = 1.017$ and $I\text{-Eff}_{\text{Rel}} = 0.879$. These values indicate that the RDR design has only a slightly worse D-efficiency, and a better I-efficiency, than the new D-optimal design for the repaired CER.

S.2 DRR Example

We now illustrate the DRR approach described in Section 3 to repair the 15-point original design and CER for this example. We chose Option 2 for the first step of the DRR approach, which involves developing acceptable replacement design points by shrinking the unacceptable design points toward the center point. For this example, it was assumed the center point from the original design was appropriate to use as a center point or baseline point for the repaired CER. Suppose that some scoping tests were performed for each of the two unacceptable design points to determine how much they must be shrunk toward the center point to obtain acceptable points. The resulting values of the shrinkage factor ($s$) for the unacceptable points in rows 1 and 5 were 0.30 and 0.45 respectively. By substituting the coordinates of the center point and each of the unacceptable points into Equation (4) along with these two values of $s$, the coordinates of the two replacement design points were calculated. The 15 points in the DRR experimental design are listed in columns A, B, and C as marked in column H of Table S.1. The two replacement design points are listed in rows 23 and 24 of Table S.1.

The second step of the DRR approach involves generating a new MVC plane for each of the replacement design points. Each MVC contains the corresponding replacement point, and is orthogonal to the line joining the replacement point to the center point. Performing the calculations as discussed in Section 3.2, the resulting MVCs are

\[
\begin{align*}
    x_1 + x_2 + x_3 & \geq 7.8 \\
    x_1 + x_2 - x_3 & \geq 0.7
\end{align*}
\]  

(S.3)
corresponding, respectively, to rows 23 and 24 in Table S.1. The MVCs exclude the two unacceptable design points and nearby portions of the original CER. Hence, the DRR CER is specified by the constraints in Equations (S.1) and (S.3).

The 15-point DRR experimental design was evaluated using the approach discussed in Section 4. A new 15-point design was generated using Design-Expert (Stat-Ease 2017) using the same approach discussed at the end of Section S.1. The only difference was that the repaired CER for the DRR approach is not the same as for the RDR approach. The 15 points in the resulting new design are listed in columns A, B, and C as marked in column I of Table S.1. The values of the relative efficiencies [given in Equations (11) and (12)] of the RDR design compared to the new design for the DRR CER are $D\text{-Eff}_{\text{Rel}} = 1.060$ and $I\text{-Eff}_{\text{Rel}} = 0.928$. These values indicate that the RDR design has only a moderately worse D-efficiency, and a better I-efficiency, than the new D-optimal design for the repaired CER.