COMSOL CONFERENCE
2018 BOSTON

Multi-objective Optimization of Microneedle Design for Transdermal Drug Delivery

M. Sarmadi[1,2,*], K. McHugh[2], R. Langer[1,2,3], A. Jaklenec[2]

1. Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA

2. David H. Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, USA

3. Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA

Presentation Outline

1. Why Microneedles?
2. Simulating approach
   - Modeling description
   - Results
3. Multi-objective optimization
   - Approach description
   - Results
4. Sensitivity analysis results
5. Questions and discussion

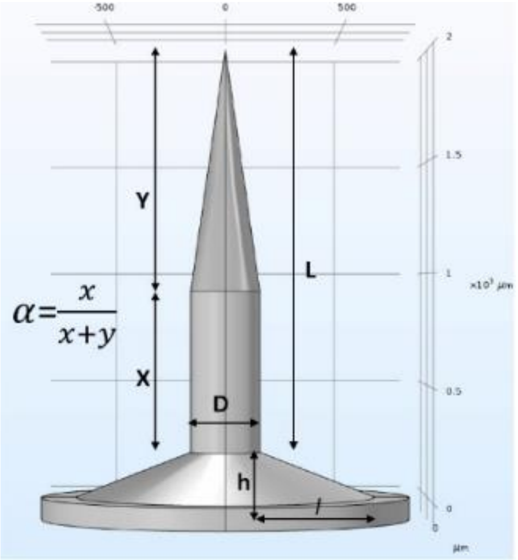
Why Microneedles?

- Less pain perception
- Safer
- Can be administrated by the patient
- Versatile fabrication techniques available

- Objective of the current study:
  - Systematic study, optimization and sensitivity analysis of the effect of microneedle geometrical parameters on mechanical stability

Simulation Approach

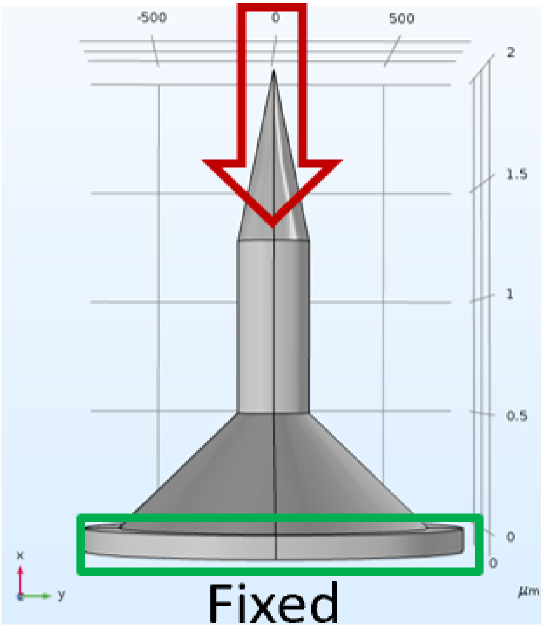
- **Geometry** of a typical microneedle was parametrized in COMSOL Multi-physics ®
- Microneedle was considered **solid** made from Poly(methyl methacrylate) or **PMMA**
- **Buckling**, **bending**, and **axial loading** considered as three loading conditions
- **Structural mechanics module** coupled with **parametric sweep** in COSMOL V5.3 ® was used for simulations



Parameter name	Parameter value list	Parameter unit
alpha	range(0.1,0.1,0.9)	
D	150,300,450	um
l	10,100,200,300,400	um
h	10,200,400,600	um
L	1000,1500,2000,2500	um

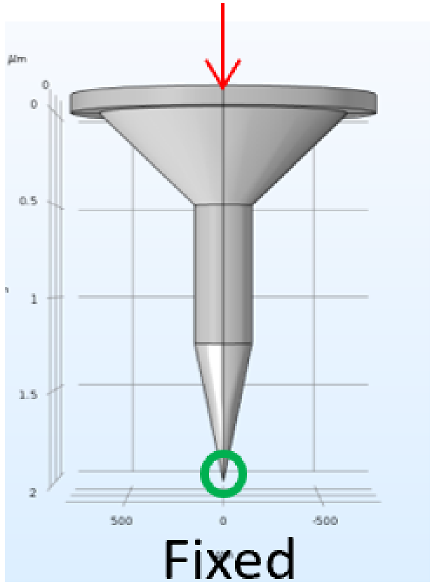
Axial loading

3.18 MPa Pressure



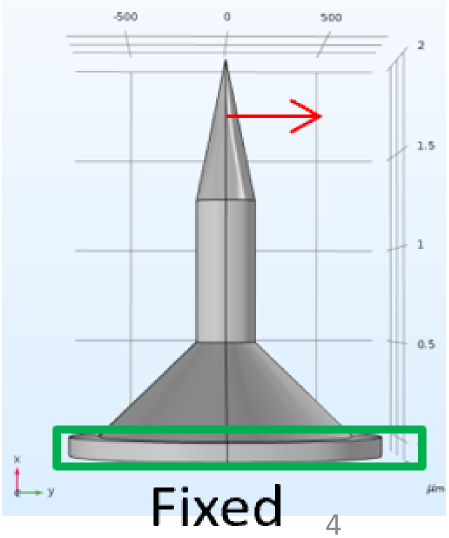
Buckling

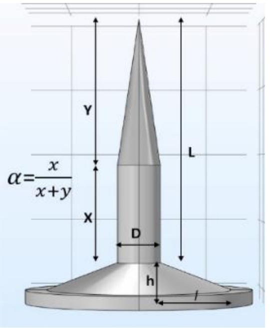
5 N Point Load



Bending

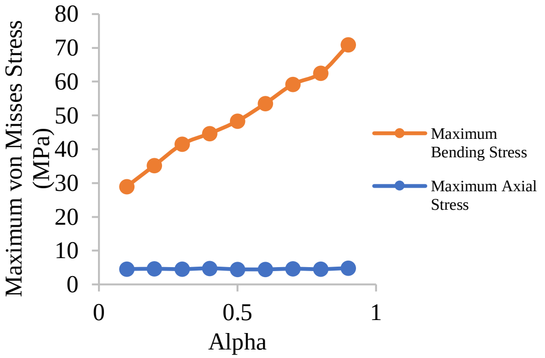
20 mN Total Load

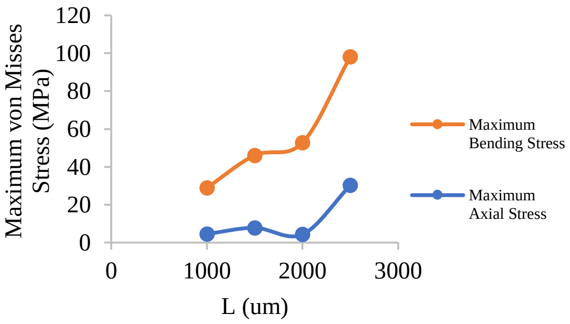


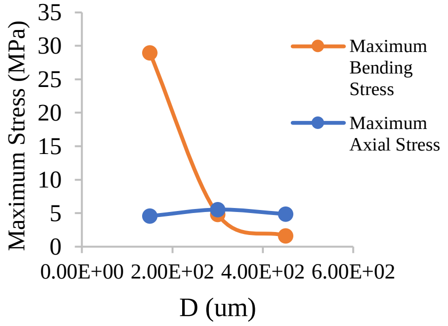


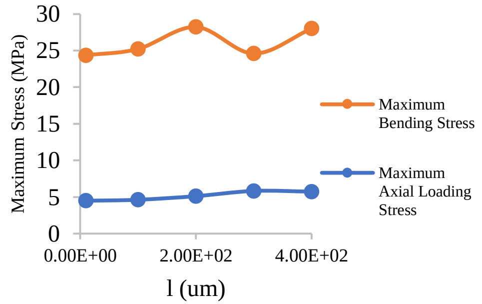
Results (Bending and Axial Loading)

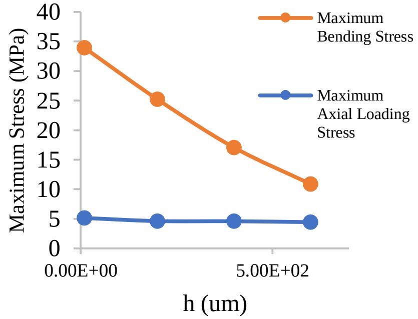
Alpha **L** **D** **l** **h**

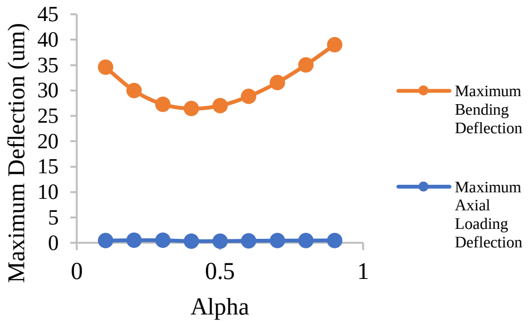


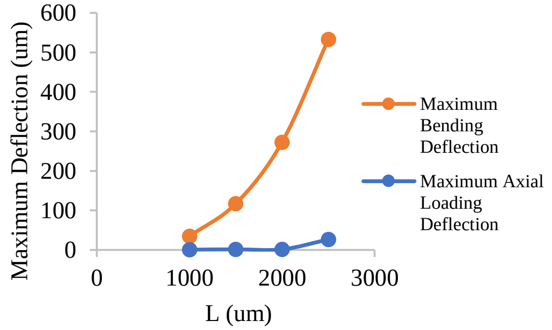


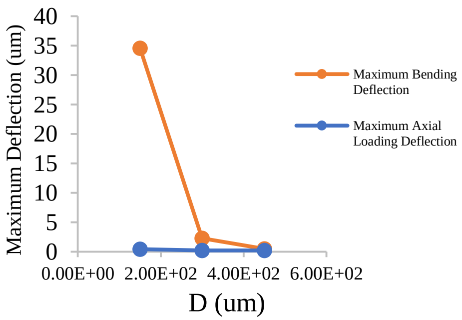


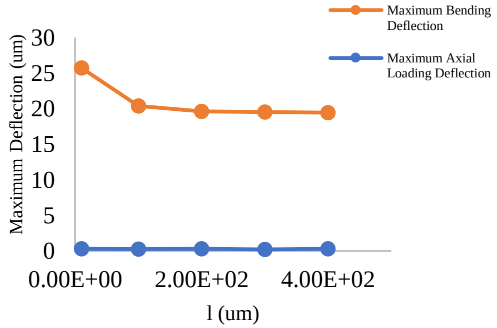


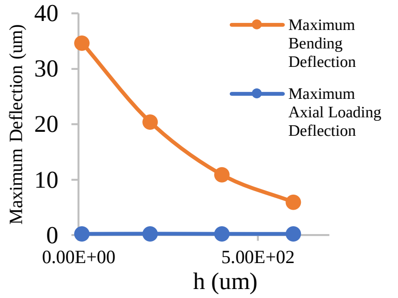




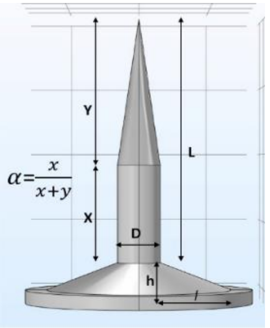






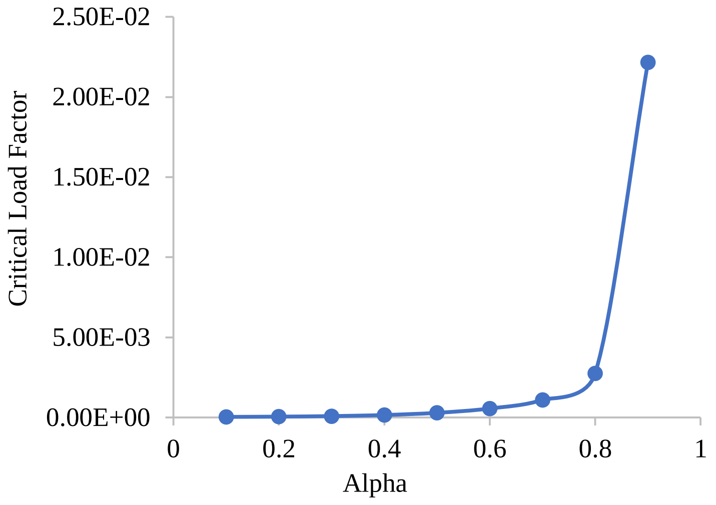


Objective functions represented a highly nonlinear behavior with respect to the considered design parameters

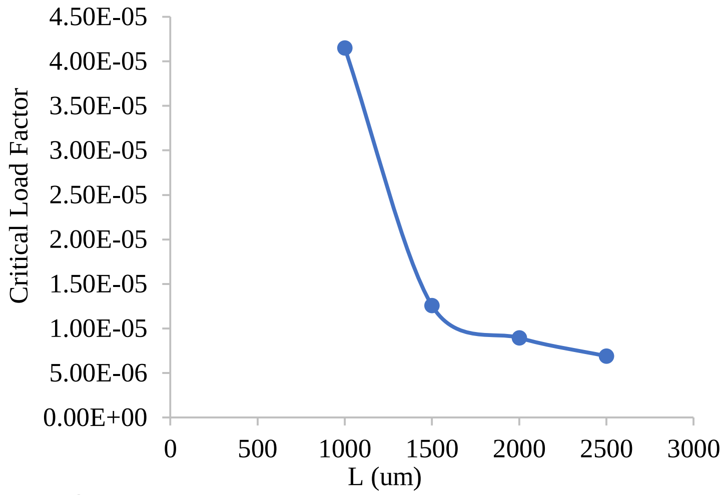


Results (Buckling)

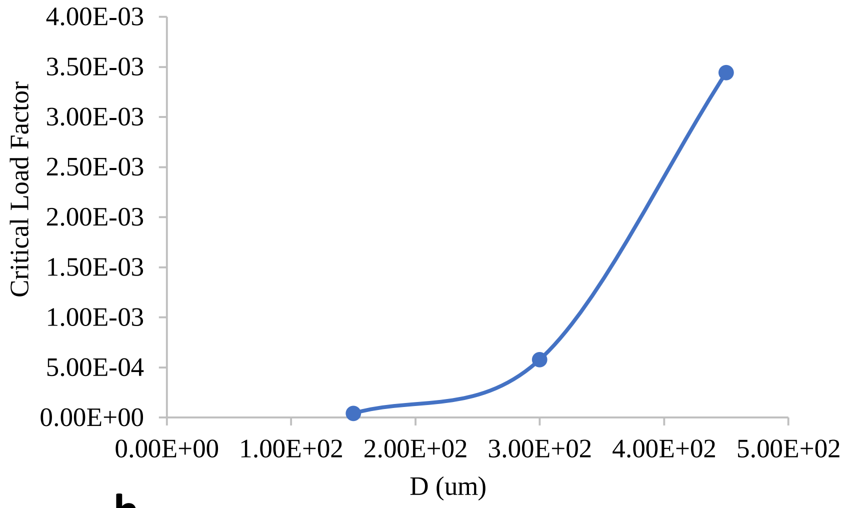
Alpha



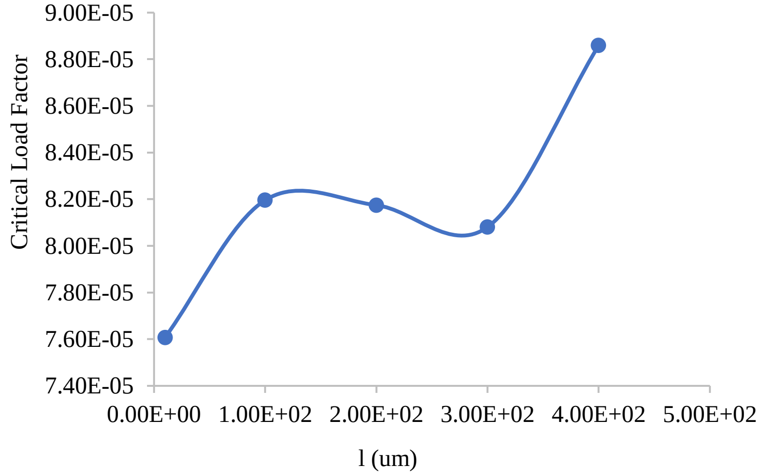
L



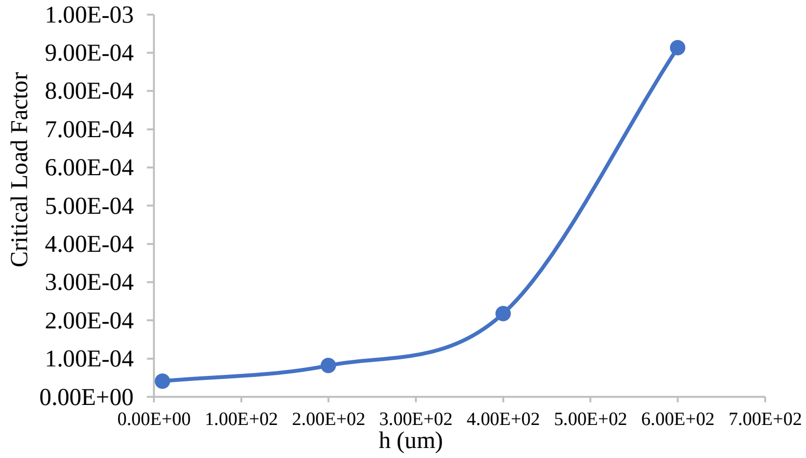
D



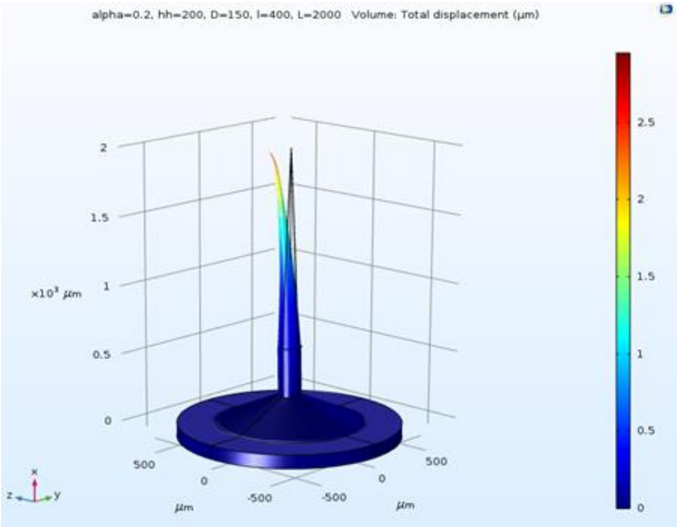
l



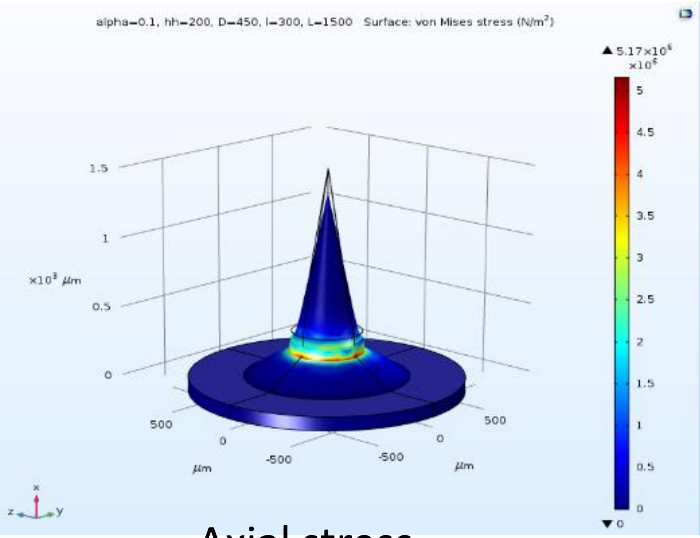
h



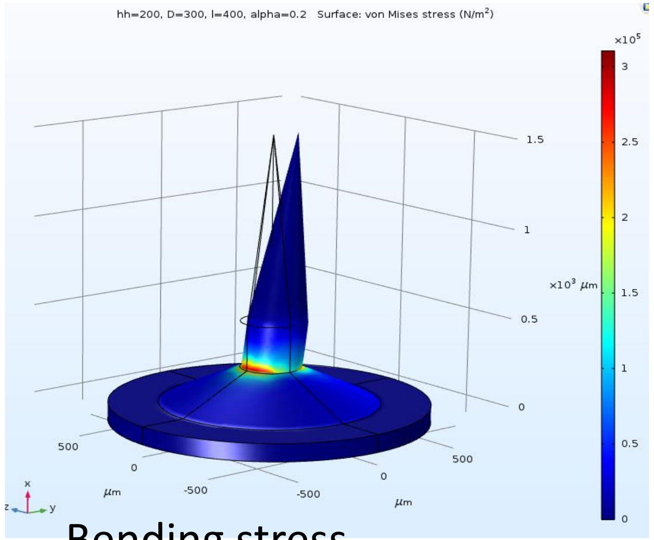
Results (Stress and Deflection Contours)



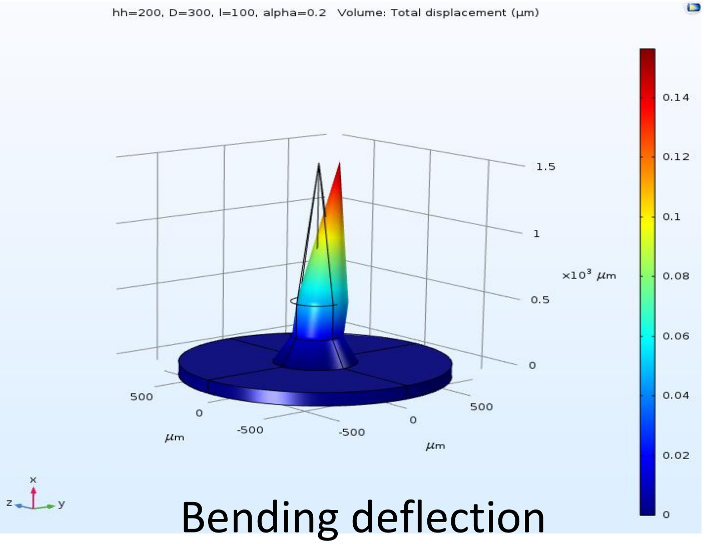
Axial deflection



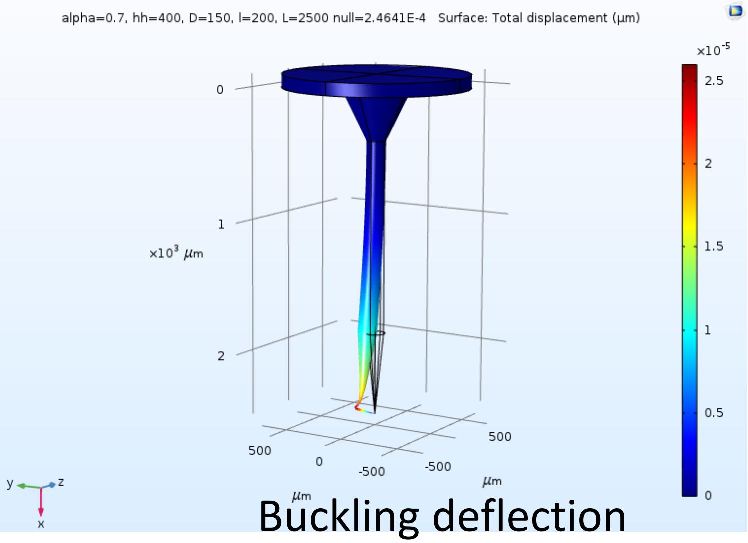
Axial stress



Bending stress



Bending deflection



Buckling deflection

Multi-Objective Optimization Approach

- Objective functions:
  - Mechanical Contribution
  1. Maximum microneedle **deflection** under **axial** loading
  2. Maximum microneedle **deflection** under **bending**
  3. Maximum von Misses **stress** under **axial** loading
  4. Maximum von Misses **stress** under **bending**
  5. **Critical buckling factor**

  - Drug delivery contribution:
  7. Microneedle shaft **volume**
- Multi-objective optimization performed using Duckstein's method [1]:

$$L_p(x) = \sum_{i=1}^{k} \left[w_i^P \left[\frac{f_i(x) - f_i^{\,0}}{f_{i,max} - f_i^{\,0}} \right]^p \right]^{1/p}$$

Results (Optimum Design Points)

- Total of **2160** simulations performed
- Top 10 optimum points for each diameter were selected
- **Shaft diameter** and **alpha** were the two major design factor
- Top 10 optimum designs corresponded to **largest alpha** and **D**

Ranking out of 2160 points	Alpha	h (um)	D (um)	l (um)	L (um)
1	0.9	4.00E+02	4.50E+02	1.00E+01	1.00E+03
2	0.9	4.00E+02	4.50E+02	1.00E+02	1.00E+03
3	0.9	4.00E+02	4.50E+02	2.00E+02	1.00E+03
4	0.9	4.00E+02	4.50E+02	3.00E+02	1.00E+03
5	0.8	6.00E+02	4.50E+02	2.00E+02	1.00E+03
6	0.9	1.00E+01	4.50E+02	1.00E+01	2.00E+03
7	0.9	4.00E+02	4.50E+02	1.00E+01	2.50E+03
8	0.8	6.00E+02	4.50E+02	3.00E+02	1.00E+03
9	0.9	4.00E+02	4.50E+02	1.00E+02	2.50E+03
10	0.8	6.00E+02	4.50E+02	1.00E+02	1.00E+03
437	0.9	6.00E+02	3.00E+02	1.00E+01	1.00E+03
440	0.9	6.00E+02	3.00E+02	3.00E+02	1.00E+03
445	0.9	6.00E+02	3.00E+02	4.00E+02	1.00E+03
504	0.9	6.00E+02	3.00E+02	1.00E+02	1.00E+03
639	0.1	2.00E+02	3.00E+02	1.00E+01	2.50E+03
641	0.1	4.00E+02	3.00E+02	1.00E+01	2.50E+03
644	0.1	6.00E+02	3.00E+02	1.00E+01	2.50E+03
646	0.9	4.00E+02	3.00E+02	1.00E+01	2.50E+03
649	0.1	1.00E+01	3.00E+02	1.00E+01	2.50E+03
1441	0.9	6.00E+02	1.50E+02	1.00E+02	1.00E+03
1442	0.9	6.00E+02	1.50E+02	2.00E+02	1.00E+03
1443	0.9	6.00E+02	1.50E+02	3.00E+02	1.00E+03
1444	0.9	6.00E+02	1.50E+02	4.00E+02	1.00E+03
1445	0.1	6.00E+02	1.50E+02	1.00E+02	1.50E+03
1446	0.2	6.00E+02	1.50E+02	1.00E+02	1.50E+03
1447	0.1	6.00E+02	1.50E+02	2.00E+02	1.50E+03
1448	0.1	6.00E+02	1.50E+02	1.00E+02	2.00E+03
1449	0.9	6.00E+02	1.50E+02	1.00E+01	1.00E+03
1450	0.1	4.00E+02	1.50E+02	1.00E+02	1.50E+03

Sensitivity Analysis

- Sensitivity analysis, based on ANOVA, was performed by Minitab ®

Source	DF	Adj SS	Adj MS	F-Value	P-Value	Percentage of contribution	Ranking
Alpha	8	1.6454	0.20568	24.03	0.00000	3.33	3
h	3	1.6356	0.5452	63.69	0.00000	3.31	4
D	**2**	**18.0386**	**9.01929**	**1053.69**	**0.00000**	**36.50**	**1**
l	4	0.0418	0.01045	1.22	0.30000	0.08	5
L	**3**	**9.7372**	**3.24573**	**379.19**	**0.00000**	**19.70**	**2**
Error	2139	18.3092	0.00856				
Total	2159	49.4077					

References:

- [1] Chiandussi, Giorgio, Marco Codegone, Simone Ferrero, and Federico Erminio Varesio. "Comparison of multi-objective optimization methodologies for engineering applications." Computers & Mathematics with Applications **63**, no. 5, 912-942 (2012).

Thank you for your time and attention!

Questions?