Electronic Supplementary Material (ESI) for Lab on a Chip.

Versatility and stability optimization of flow-focusing droplet generators via quality metric-driven design automation

David McIntyre,[a,b] Ali Lashkaripour,[c,d] Diana Arguijo,[a,b] Polly Fordyce,[c,d,e] and Douglas Densmore[*,b,f]

a. Boston University Biomedical Engineering Department, 44 Cummington Mall, Boston, USA.
b. Biological Design Center, 610 Commonwealth Ave, Boston, USA.
c. Department of Bioengineering, Stanford University, Stanford, CA., USA
d. Department of Genetics, Stanford University, Stanford, CA., USA
e. Chan-Zuckerberg Biohub, San Francisco, CA., USA
f. Boston University Electrical and Computer Engineering Department, 8 Saint's Mary St., Boston, USA.

Supplementary Table 1: Overview of all droplet generators used in this study

Device Description	Or (um)	Or_L	W_d	W_c	E	A.R	Ca	F.R.R
Orthogonal Device #1 (Figure 2)	75	1	2	2	2	1	.06-1.05	10-22
Orthogonal Device #2 (Figure 2)	75	1.5	2.5	2.5	3	1.5	.06-1.05	10-22
Orthogonal Device #3 (Figure 2)	75	2	3	3	4	2	.06-1.05	10-22
tOrthogonal Device #4 (Figure 2)	75	2.5	3.5	3.5	5	2.5	.06-1.05	10-22
Orthogonal Device #5 (Figure 2)	75	3	4	4	6	3	.06-1.05	10-22
More Versatile (Figure 3)	75	3	2	2	4.5	1	.05-1.05	2-22
Less Versatile (Figure 3)	150	1	4	4	2	3	.05-1.05	2-22
More Versatile (Figure 4)	150	2	2	2	5	1	.05-1.05	2-22
Less Versatile (Figure 4)	175	1.5	2.5	2.5	2	1	.05-1.05	2-22
More stable (Figure 5)	175	3	2	2	3.5	1.5	.05-1.05	2-22
Less stable (Figure 5)	75	1	3.5	3.5	2	3	.05-1.05	2-22
More stable (Figure 6)	175	2.5	3	2.9	6	1	.05-1.05	2-22
Less stable (Figure 6)	175	3	3.3	3	2	1.5	.05-1.05	2-22

Abbreviations: **Or -** orifice width; **Or_L** -normalized orifice length; **W_d –** normalized dispersed phase (water) input; **W_c** – normalized continuous phase (oil) input; **E** – Expansion ratio; **A.R** – Aspect ratio; **Ca** - capillary number; **F.R.R –** Flow rate ratio

Supplementary Table 2: Correlation coefficients (R^2) for design parameters and versatility scores in the dripping regime

	Or (um)	Or_L	W_d	W_c	E	A.R
Overall Score	-0.19	0.41	-0.13	-0.18	0.17	-0.51
Size Score	0.57	-0.06	-0.01	-0.20	-0.02	0.58
Rate Score	-0.53	0.39	-0.05	-0.03	0.012	-0.60

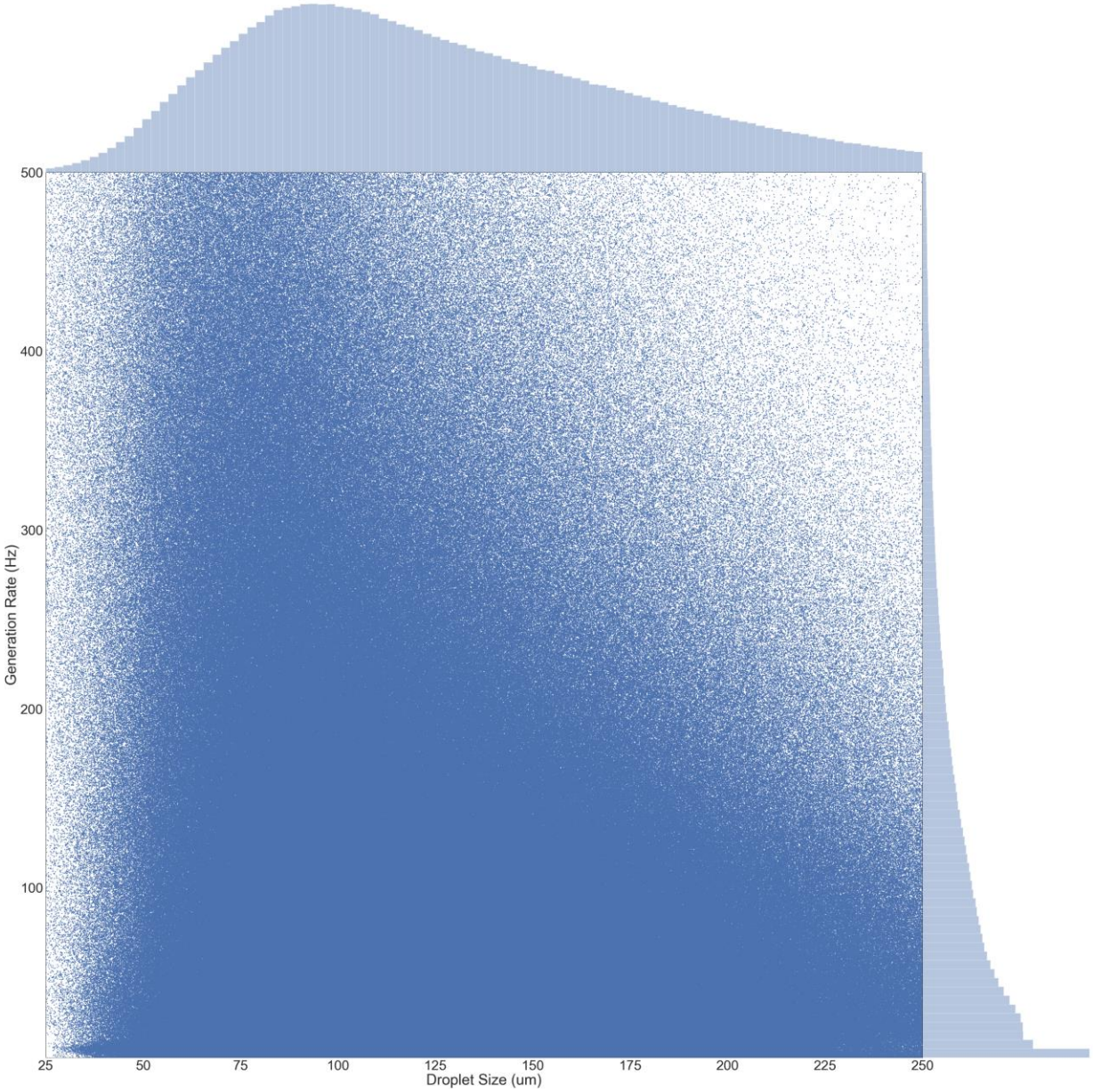
Interpreting R^2 values: **$-1.0 < R^2 < -0.7$** – strong negative correlation; **$-0.7 < R^2 < -0.5$** – moderate negative correlation; **$-0.5 < R^2 < -0.3$** – weak negative correlation; **$-0.3 < R^2 < 0.3$** – negligible correlation; **$0.3 < R^2 < 0.5$** – weak positive correlation; **$0.5 < R^2 < 0.7$** – moderate positive correlation; **$0.7 < R^2 < 1.0$** – strong positive correlation

Supplementary Table 3: Correlation coefficients (R^2) for design parameters and versatility scores in the jetting regime

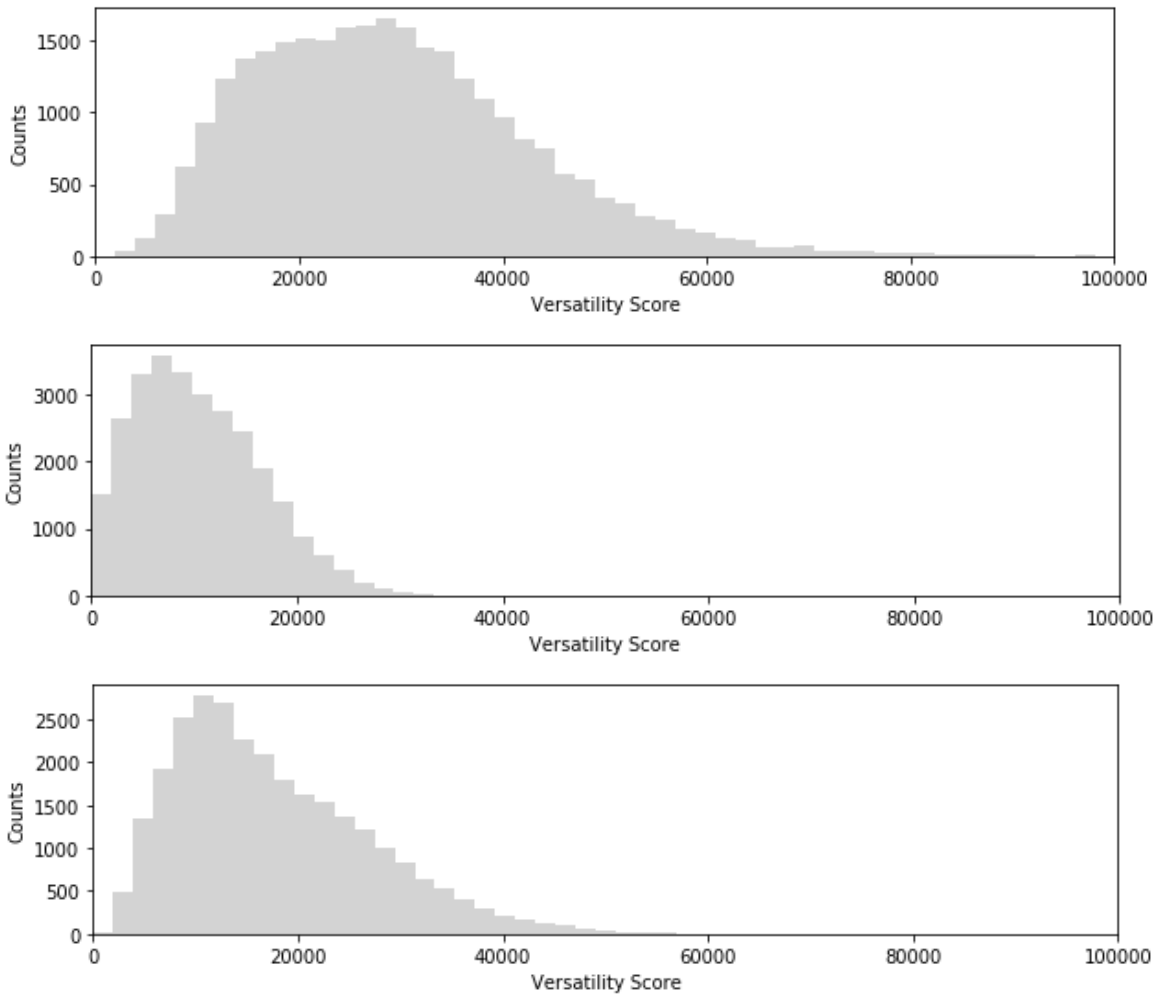
	Or (um)	Or_L	W_d	W_c	E	A.R
Overall Score	-0.05	0.06	-0.58	0.33	-0.35	-0.05
Size Score	0.54	-0.15	-0.10	-0.23	0.66	0.26
Rate Score	-0.29	0.08	-0.46	0.3	-0.59	-0.18

Supplementary Table 4: Correlation coefficients (R^2) for design parameters and stability scores in the dripping and jetting regime

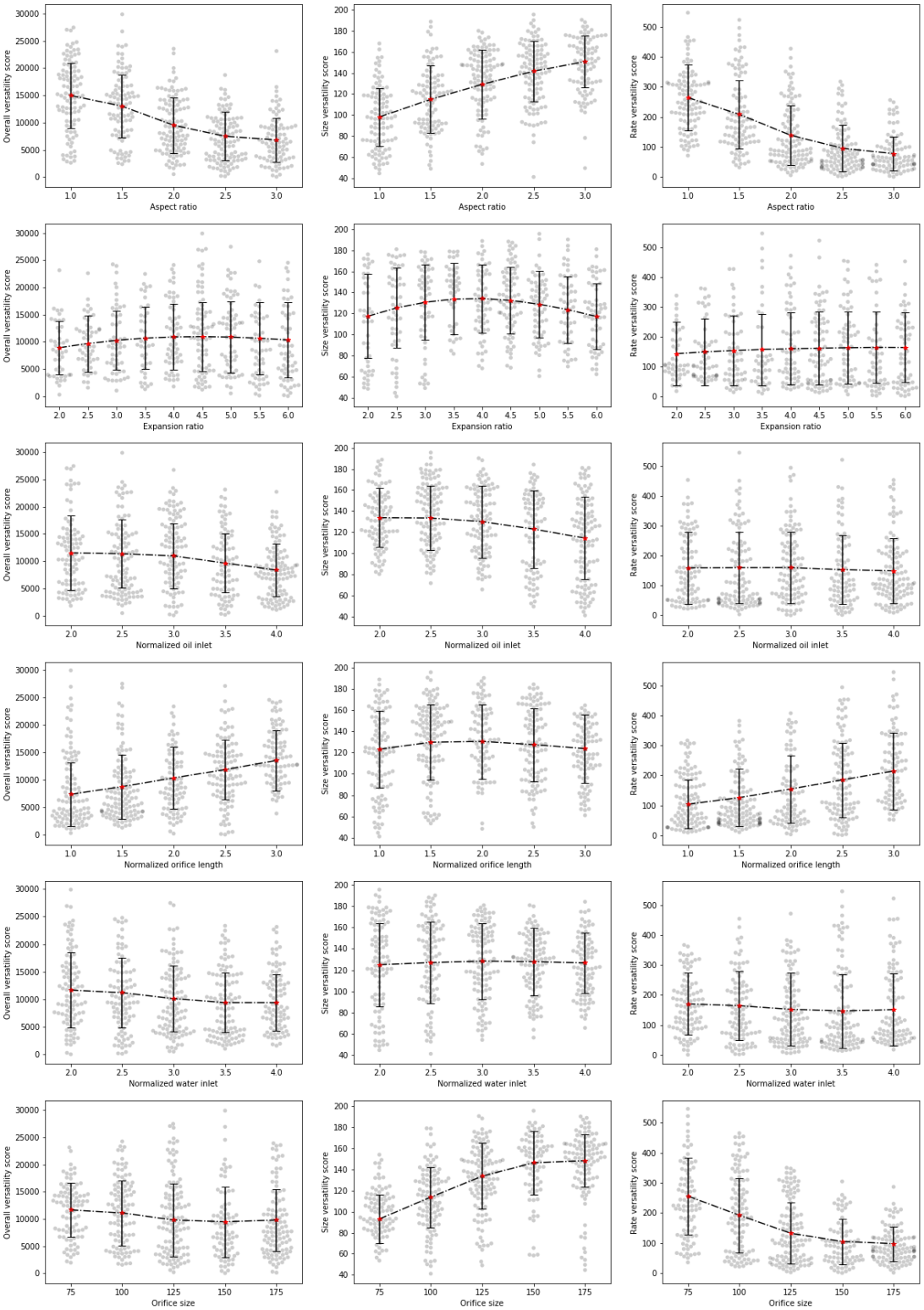
	Or (um)	Or_L	W_d	W_c	E	A.R	Ca	F.R.R
Dripping	0.54	0.16	-0.10	0.09	0.09	0.06	-0.21	0.01
Jetting	0.47	0.02	-0.26	0.17	0.00	0.33	0.46	-0.06



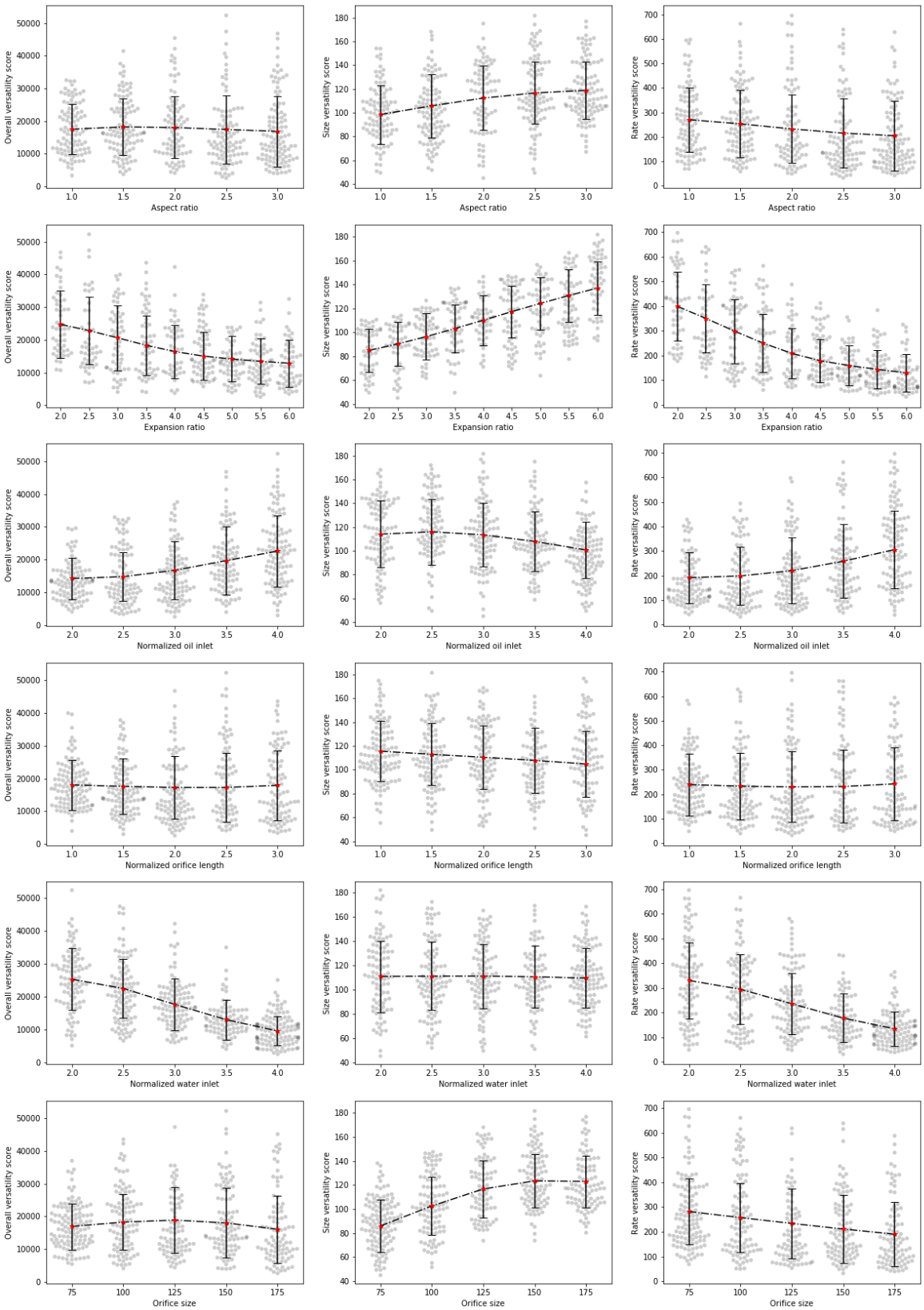
Supplementary figure S1: *2D distribution of droplet size and rate from the 4.2 million datapoints used in this study.*



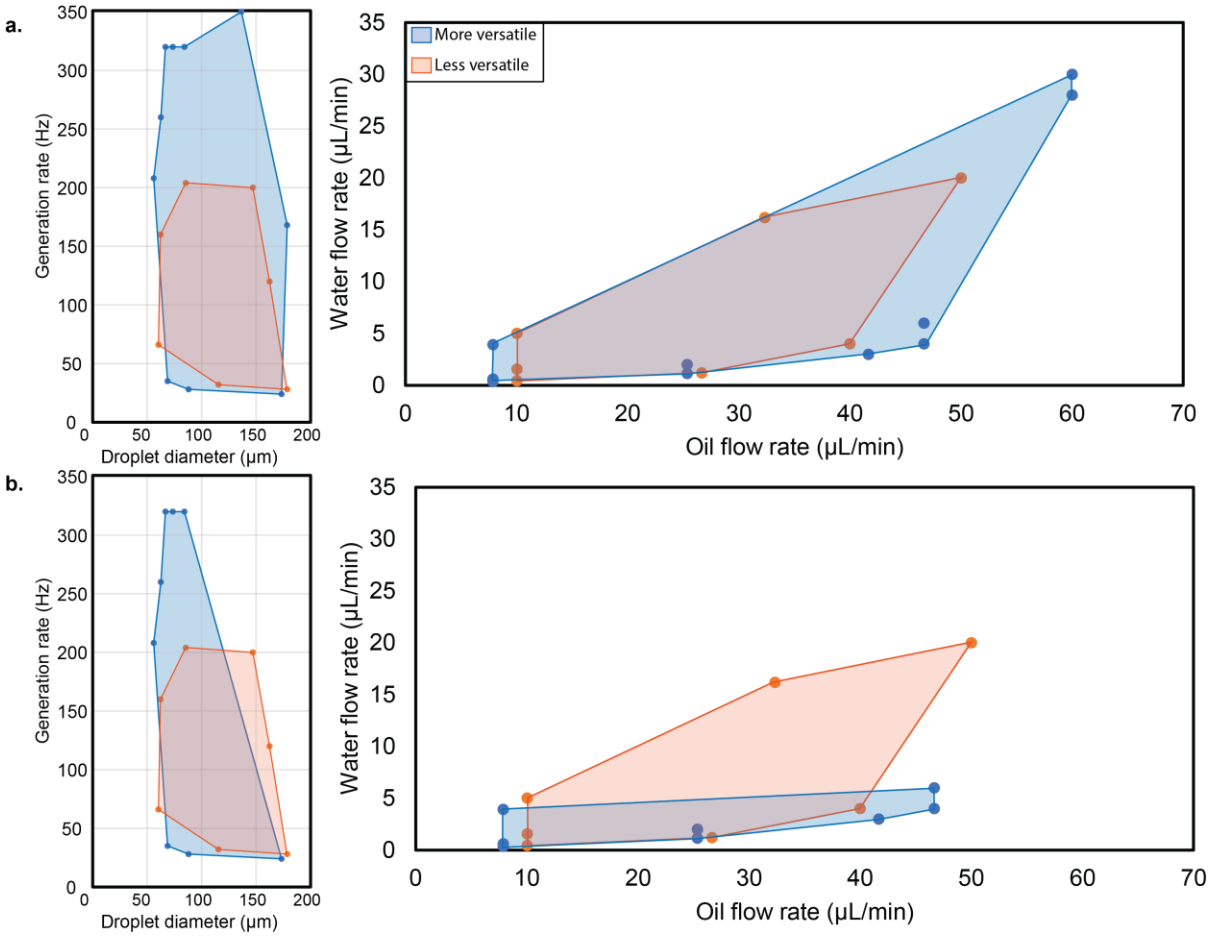
Supplementary Figure S2: Distribution of versatility scores in both regimes (top), dripping regime (middle), and jetting regime (bottom).



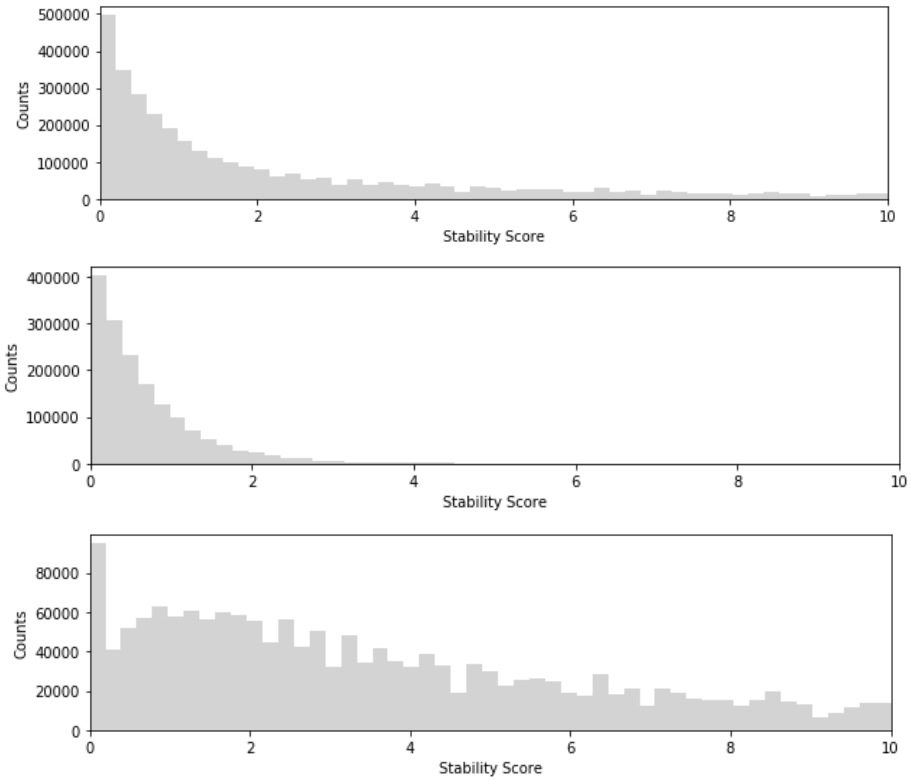
Supplementary Figure S3: Diameter, generation rate, and overall versatility in the dripping regime.



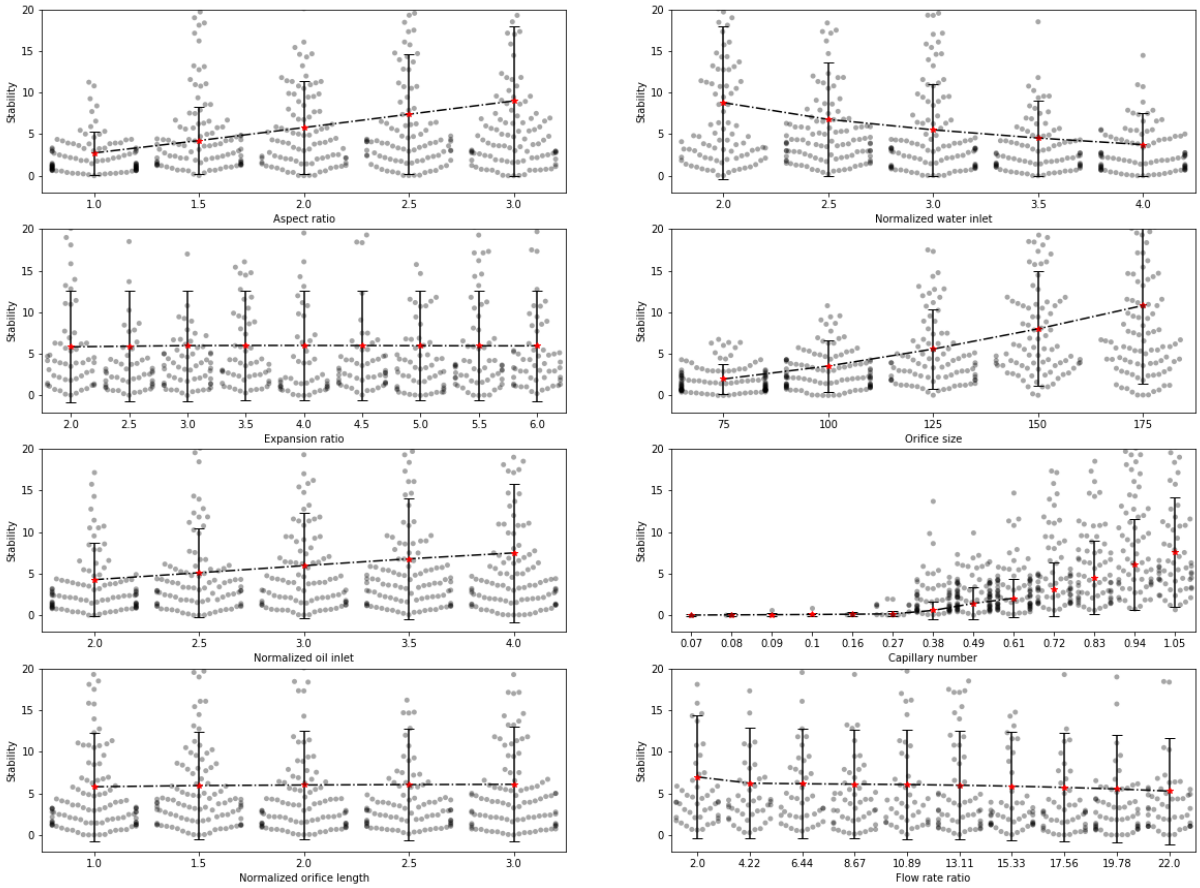
Supplementary Figure S4: Main effect analysis of diameter, generation rate, and overall versatility in the jetting regime.



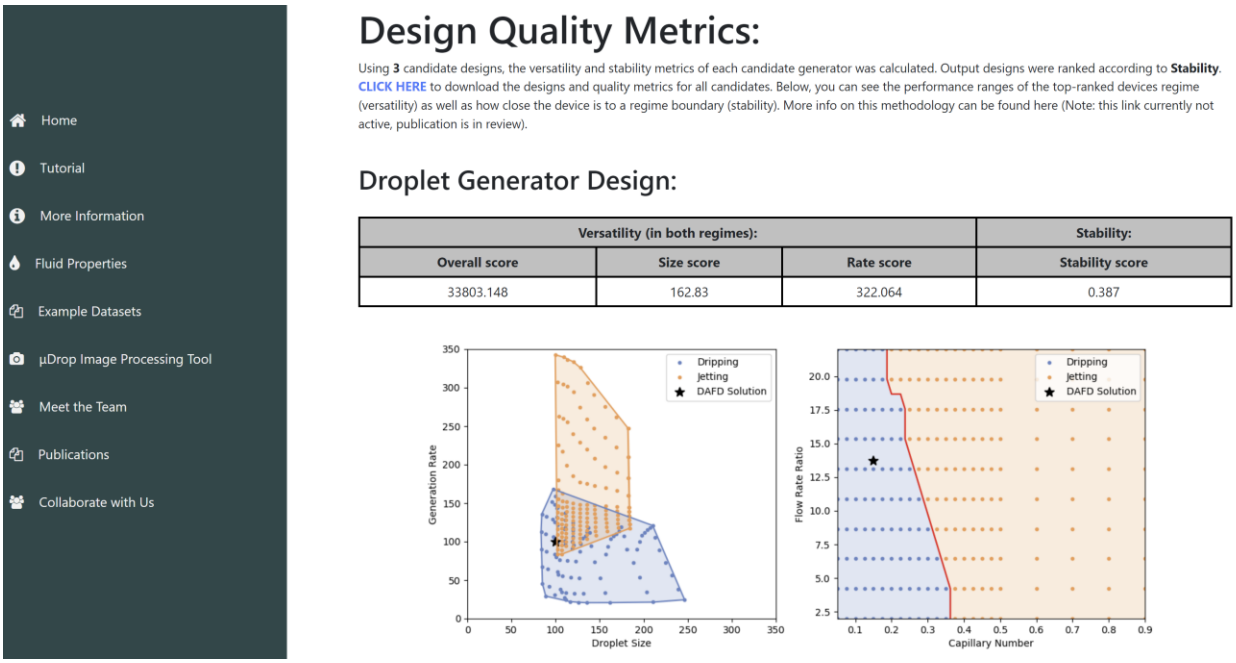
Supplementary Figure S5: Summary of flow rate combinations used for the more and less versatile devices in main figures 2 and 3



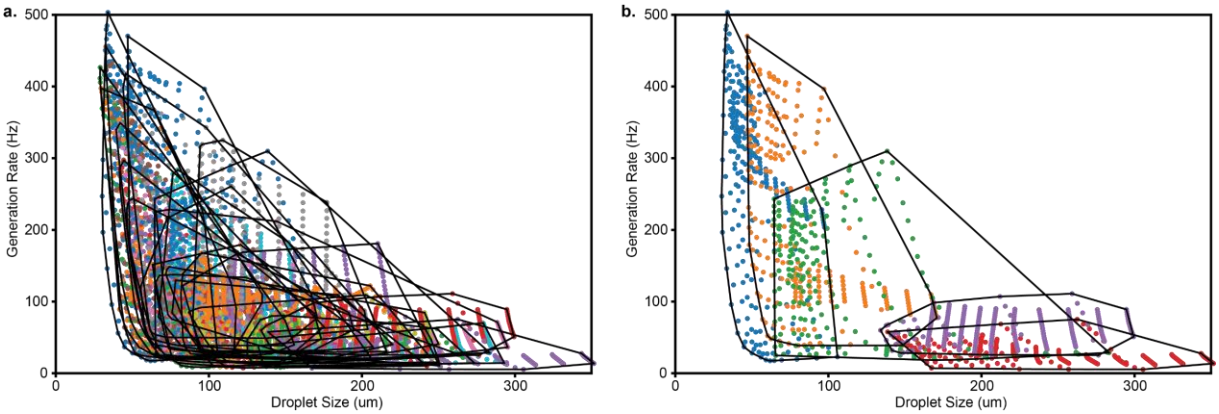
Supplementary Figure S6: Distribution of stability scores in both regimes (top), dripping regime (middle), and jetting regime (bottom).



Supplementary Figure S7: Main effect analysis of stability in the jetting regime.



Supplementary Figure S8: DAFD Quality metric design report. If specified by the user, upon completion of metrics-driven design automation, a companion report will be generated to contextualize the results for the user.



Supplementary Figure S9: Design space coverage of (a) the 25 orthogonal devices used in DAFD and (b) a selection of 5 of the orthogonal devices that can cover more than 99% of the design space.