Supporting Information

Combinatorial microneedle patch with tunable release kinetics and dual fast-deep/sustained release capabilities

Miguel Angel Lopez-Ramirez,^a Daniel Kupor,^a Leonardo Marchiori,^a Fernando Soto,^a Ricardo Rueda,^a Maria Reynoso,^a Lakshmi Rekha Narra,^b Krishnan Chakravarthy^{*a,b} and Joseph Wang^{*a}

^a Department of Nanoengineering, University of California, San Diego, La Jolla, California 92093, United States.

^b Department of Anesthesiology and Pain Medicine, University of California, San Diego, Health Sciences, La Jolla, California, 92093, United States.

* Correspondence to: kvchakravarthy@health.ucsd.edu and josephwang@ucsd.edu

Supporting Tables

Table S1. Lithographic 3D printing parameters of MN arrays: variable layer thickness.

Table S2. Lithographic 3D printing parameters of MN arrays: variable angle.

Table S3. PDMS micromolding and post curing parameters.

Supporting Figures

Fig. S1 Lithographic 3D printed MNs.

Fig. S2 Lithographic 3D printed MN tip sharpness.

Fig. S3 Heat exchange (temperature change) from Mg microparticles

Fig. S4 UV-vis absorbance curves of the release of combinatorial MN patches.

Fig. S5 PLGA microparticle sustained release approach.

Fig. S6 Sustained release MN detachment from the base of the patch



Fig. S1 Lithographic 3D printed MN master arrays fabricated via mask photolithography: (a) 20 μ m layers, (b) 50 μ m layers, both printed at an angle of 0 deg (no supports).



Fig. S2 Lithographic 3D printed MN tip sharpness (20 μ m layer thickness): (a) support angle 55 deg, (b) support angle 45 deg, (c) support angle 30 deg.



Fig. S3 Heat exchange (temperature change) from different amount of Mg microparticles (0.5, 2, 3, 7, and 10 mg) in 300µL of PBS solution, pH 3.0 (a) and 7.4 (b).



Fig. S4 UV-vis absorbance curves of the release of combinatorial MN patches: fast acting MN compartment 3% CMC-FITC (fixed) + variable Eudragit[®]L100/Rh6G (4-24%)



Fig. S5 PLGA microparticle sustained release approach. (a) PLGA microparticle formulation. (b) SEM of PLGA microparticles. Scale bar, 10 μ m. (c) Fluorescence microscopy image (RFP channel) of PLGA microparticles loaded with Rh6G. Scale bar, 20 μ m. (d) Cumulative release curve of Rh6G from PLGA microparticles.



Fig. S6 Sustained release MN detachment from the base of the patch, and "fast-acting" MN dissolution. Scale bar, 2.5mm.

Layer (mm)	Thickness	Exposure Time (s)	Off time (s)	Bottom Exposure (s)	Bottom Layers	Support Angle
0.02		10	3	80	25	0
0.05		10	3	80	10	0
0.1		10	3	80	5	0

Table S1. Lithographic 3D printing parameters of MN arrays: variable layer thickness (20-100 μm), no

angle.

Layer Thickness (mm)	Exposure Time (s)	Off time (s)	Bottom Exposure (s)	Bottom Layers	Support Angle	Tip Sharpness
0.02	10	3	80	25	55	~20µm
0.02	10	3	80	25	45	~20µm
0.02	10	3	80	25	30	~20µm

thickness.

3D printed mold heating (ºC)	Exposure Time (min)	PDMS base:curing agent	PDMS curing temperature(ºC)	PDMS curing time	Result
120	3	84:16	85	30 min	PDMS Curing Process Inhibited
120	5	84:16	85	30 min	-
120	10	84:16	85	30 min	-
120	15	84:16	85	30 min	-
120	20	84:16	85	30 min	Mold cured correctly
120	25	84:16	85	30 min	+
120	30	84:16	85	30 min	+
120	30	84:16	Room Temperature	24 hours	+

Table S3. PDMS micromolding and post curing parameters: temperature and UV exposure time.