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Functional material-mediated wireless physical stimulation for neuro-modulation and regeneration

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Table S1 Overview of the functional materials for wireless physical stimulation.

Stimulation type	Biomaterial	Feature	Stimulation parameter	Cell/animal response	Ref.
Piezoelectric stimulation	PVDF	A nanopillar array fabricated by hot-pressing	US, 5 min, 2 times a day, 300-500 W	Neuron-like differentiation of rBMSCs	1
	BZT-BCT/PVDF	Thin films fabricated by electrospinning of the composite containing PVDF and BZT-BCT nanowires	US, 1 MHz, pulse width 5 ms, pulse interval 100 ms, acoustic pressure 150 kPa	The generation of CMAPs and the twitching of limbs	2
	KNN/PLA	A biodegradable 3D multichannel nanofiber scaffold	US: (1) *In vitro*: 20 min, 1 MHz, 0-150 kPa; (2) *In vivo*: 20 min every 2 days, lasted for 4 weeks	(1) Neuronal differentiation of NSCs; (2) Neuro-regeneration and functional recovery of SCI rats	3
	BN	BN nanotubes prepared by annealing can be internalized by cells	US, 20 W, 40 kHz, for 5 s, 4 times a day for 9 days	Promoted neurite outgrowth of PC 12 cells	4
	BTNPs	Tetragonal BTNPs	US, 1 MHz, 0.1-0.8 W/cm^2	US induced calcium transient in SH-SY5Y cells	5
	BTNP-PDA-BNN6	US-driven release of NO, allowing the BBB penetration	US: (1) *In vitro*:2.2 MHz, 10 s, 0.4 W/cm^2, (2) *In vivo*: 1.5 MHz, 462.4 W/cm^2, duty cycle: 10%, pulse repetition frequency: 10 Hz, 66.4 W/cm^2	(1) Increased Ca^{2+} influx and dopamine release of SH-SY5Y cells; (2) Alleviated symptoms of the mice with PD	6

ME stimulation	$CoFe_2O_4$@$BaTiO_3$	Core-shell MENPs can be stereotactically injected into deep brain	(1) *In vitro*: 225 mT (DC MF), 6 mT, 140 Hz (AC MF); (2) *In vivo*: 220 mT (DC MF), 6 mT, 140 Hz (AC MF), 180 s	(1) Induced Ca^{2+} transient f SH-SY5Y; (2) Increased expression of c-Fos *in vivo* and controlled mouse behavior	7
	FO@BTO/AHA hydrogel	Core-shell MENPs were combined with biomimetic hydrogel with features of native neural ECM	Pulsed MF (13 mT, 60 Hz, duty cycle of 50%), 0.5 h per day	(1) Promoted neurogenesis of PC 12 cells *in vitro*; (2) facilitated neuro-regeneration in SCI rats	8
	GO/CFO/PVDF	ME nanofiber films prepared by electrospinning	EMFs, 1 mT, 50 Hz, 8 h/day for 21 days	Neuron-like differentiation of MSCs	9
	Metglas/PVDF or PZT	The nanogenerators were implanted into the STN of rats with PD, ensuring ME stimulation in freely moving rats	AMF, 1.5 mT, 1 min, 200 Hz, biphasic pulses	Decreased rotation rate of the rats with PD	10
	Metaglas/PZT	The ME film can be implanted directly and delivered through a percutaneous catheter to big animals	AMF, <1 mT, 3 V, 1.5 ms pulse width monophasic, 1-10 Hz	Induced CMAPs of rats and pigs	11
Optoelectrical stimulation	Silicon	Nanoporous/non-porous silicon heterojunctions fabricated by metal-free etching	532 nm laser: 10 ms, 8-68 mW/mm^2; 808 nm laser:10 ms, 15-209 mW/mm^2	*In vivo* sciatic nerve simulation induced the generation of APs and leg displacement of rats	12
	Silicon	Silicon structures, including nanowires, membranes and meshes for multiscale stimulation *in vitro* and *in vivo*	(1) For cells: 592 nm, 14.4 mW, 237 nm spot size, 1 ms; (2) For brain slice: 473 nm, 1 ms, 2 mW, 57 µm spot size; (3) *In vivo* photo-stimulation: 473 nm, 4-5 mW, 216 µm spot size	(1) Induced intracellular Ca^{2+} influx in both DRG and glial cells; (2) Generation of excitatory postsynaptic currents in brain slices; (3) Evoked small ipsilateral forelimb movements	13

	P3HT	Photovoltaic layer prepared by spin-coating	(1) *In vitro*: 532 nm, 20 ms, 15 mW/mm^2, 1-20 Hz; (2) *In vivo*: 532 nm, 10 ms, 4 mW/mm^2	(1) Induced the generation of APs in primary neurons; (2) Restored light-responses in blind retinas	14
	P3HT/collagen or collagen/hyaluronan hydrogels	Hydrophilic P3HT NPs were integrated into biomimetic hydrogels to create a neural interface and a 3D biomimetic stem cell niche	530 nm pulsed light, 6 mW/cm^2, 500 ms duration, 1 Hz, 30 min/12 h	(1) Promoted growth of primary neurons; (2) Enhanced neuronal differentiation of BMSCs	15
Magetothermal stimulation	$MnFe_2O_4$	The $MnFe_2O_4$ NPs (d=6 nm) were conjugated with streptavidin for specific targeting	RF magnetic field (40 MHz, 8.4 G, 30 s)	TRPV1 opening and activation of APs in HEK 293 cells;	16
	Fe_3O_4	MNPs were modified with PEG shell	AMF, f=500 kHz, H_o =15 kA/m	(1) Evoked correlated trains of APs in neurons *in vitro*; (2) Increased expression of c-Fos *in vivo*	17
	Co-Mn-Ferrite	Core-shell MNPs	AMF: (1) *In vitro*: 412.5 kHz, 22.4 kA/m, 5 s; (2) *In vivo*: 570 kHz, 7.5 kA/m, 1 min	(1) Elicited AP firing in neurons; (2) Increased angular velocity of movement in a mouse model	18
Photothermal stimulation	Gold	Gold nanostars prepared by a modified seedless and surfactant free method	785 nm laser, 3-15 mW/mm^2, 10 s,	Inhibition of neuronal activity	19
	Graphene	A nanowire-templated 3D fuzzy graphene	405 nm laser, 1.2 ms pulse duration, 1.45-3.02 mW, 1-20 Hz	Highly controlled activation of APs in DRG neurons	20
	PDA/collagen	PDA NPs were integrated with collagen to prepare a photothermal 3D foam	808 nm laser, 6 mW/mm^2, 10-30 s duration	Suppressed spike rate of neurons	21

	Gold	Gold nanorods	980 nm laser, 1 ms duration, 0.159-1.046 J/cm^2,	Elicited compound nerve APs of rat sciatic nerves	22
Photoacoustic stimulation	ZnO/epoxy @ graphite/epoxy	A fiber-optoacoustic convertor with tip composed of ZnO/epoxy @ graphite/epoxy double-layer structure used for photoacoustic stimulation	1030 nm laser, 3 ns pulse width, 100 μJ, 3.6 kHz, 200 ms	(1) Induced Ca^{2+} transient in primary neurons; (2) Induced neural activation in mouse brain	23
	CNT/PDMS	CNT/PDMS act as the light absorption/thermal expansion layer	1030 nm laser, 3 ns pulse width, 11.4 mW, 1.7 kHz, 1 and 50 ms duration	Activation of a single neuron or subcellular structures	24
	Polystyrene-block-poly (acryl acid)	The photoacoustic nanotransducers can be conjugated with targeting antibodies	1030 nm laser, 3 ns pulse width, 3.3 kHz, 3 ms, 2.1 mJ/cm^2 (*in vitro*), 21 mJ/cm^2 (*in vivo*)	(1) Transient activation of neurons; (2) Induced local field potential in brain of mice	25
	PANIP-ES@AOT	The nanovesicles were prepared by HRP/H_2O_2-trigged polymerization on AOT vesicles	(1) *In vitro*: 1064 nm, 40 μJ, 10 ms pulse width, (2) *In vivo*: 1064 nm, 40 μJ, 10 s pulse width, 20 Hz, 10 s	(1) Ca^{2+} transient in DRG neurons; (2) Increased neuronal firing rates in mouse hippocampus and motor cortex and induced fast motion of mice	26
	CNT/silk	Photoacoustic scaffold was prepared by embedding PEG-functionalized CNTs into silk	1030 nm laser, 3 ns pulse width, 1.7 kHz, 8.8-23.5 μJ, 5 ms duration, every 2 min within total duration of 1 h	Induced Ca^{2+} transient, promoted neurite outgrowth of DRG neurons and increased expression of BDNF and NGF	27
Optogenetic stimulation	$NaYF_4$:Yb^{3+}/Tm^{3+}@ $NaYF_4$ (UCNP)/PCL	The UCNPs were combined with collagen-modified PCL scaffold by electrospinning and electrospraying	980 nm laser, 800 mW/cm^2, 500 ms pulse width, 1 Hz, 10 min/12 h;	Promoted neurite extension of PC 12 cells expressing CatCh	28

	$NaYF_4$:Yb/Tm@SiO_2	Silica was used to decorate UCNP to optimize the biocompatibility and long-term utility	980 nm laser: (1) *In vitro*: 0.35-8.22 W/mm^2, 10-50 Hz; (2) *In vivo*: 15-ms pulses at 20 Hz, 700 mW peak power (3) *In vivo*: 15-ms pulses at 8 Hz, 3.0 W peak power, 360 mW average power	(1) Evoked spikes in neurons expression ChR2 *in vitro*; (2) Increased expression of c-Fos and release of dopamine *in vivo*; (3) Induced hippocampal local field potential *in vivo*	29
	$NaYF_4$:Yb/Er@ $NaYF_4$ (UCNP)/polypropylene (PP)	The UCNP was combine with PP and implanted at the spinal cord of mice	980 nm laser, 20 mW/mm^2, 0.5 and 1 Hz, 50 ms pulse width,	Induced muscular activity in ChR2-transfected mice and inhibited movement	30
Magnetomechanical stimulation	Zinc doped iron oxide ($Zn_{0.4}Fe_{2.6}O_4$)	Octahedral $Zn_{0.4}Fe_{2.6}O_4$ NPs assemble into m-Torquer that is used to generate torque force when exposed to a rotating magnetic field generated by a circular magnet array (CMA)	Rotating CMA: 0.5 s pulse duration, 0.5 Hz, 90 degree turn	(1) Induced Ca^{2+} influx in neurons; (2) *In vivo* stimulation activated mouse motility	31
	Fe_3O_4	Magnetite nanodiscs were produced by reducing hematite to magnetite	Magnetic field, 1-5 Hz, 7-28 mT, 4 pulses of 10 s at intervals of 30s.	Increased Ca^{2+} influx in HEK-293 cells expressing TRPV4	32
	Mercaptan-functionalized magnetic particles/HA hydrogel	3D magnetic hydrogel composed of hyaluronan with similar biochemical and biophysical properties to brain tissue	Magnetomechanical stimulation (calculated): 0.136 Hz, 0.15 to 1 μN, 30 min/day, 4 days	Increased Ca^{2+} influx in DRG neurons	33
	$Zn_{0.4}Fe_{2.6}O_4$@SiO_2@pNiPMAm hydrogel nanoparticles	$Zn_{0.4}Fe_{2.6}O_4$ converts magnetic anisotropic energy to thermal energy to induce the pNiPMAm contraction	AMF, 500 kHz at 500 Oe, 30 s ON/2 min OFF cycle for 15 times	Activation of the Notch signaling in Notch1-U2OS cells	34

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