Supplementary information

A responsive cascade drug delivery scaffold adapted to the therapeutic time window for peripheral nerve injury repair

Yizhu Shan [‡abc], Lingling Xu [‡d], Xi Cui [ac], Engui Wang [a], Fengying Jiang [ae], Jiaxuan Li [a], Han Ouyang [c], Tailang Yin [f], Hongqing Feng [*ac] , Dan Luo [*ac], Yan Zhang [*b], Zhou Li [*ac]

[a] Beijing Institute of Nanoenergy and Nanosystems, Chinese Academy of Sciences, Beijing 100083, China

[b] Department of Clinical Laboratory, Renmin Hospital of Wuhan University, Wuhan 430060, China

[c] School of Nanoscience and Engineering, Chinese Academy of Sciences, Beijing 100049, China

[d] CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety & CAS Center for Excellence in Nanoscience, National Center for Nanoscience and Technology of China, Beijing 100190, China

[e] Center on Nanoenergy Research, School of Physical Science and Technology, Guangxi University, Nanning 530004, China

[f] Reproductive Medicine Center, Renmin Hospital of Wuhan University, Wuhan 430060, China

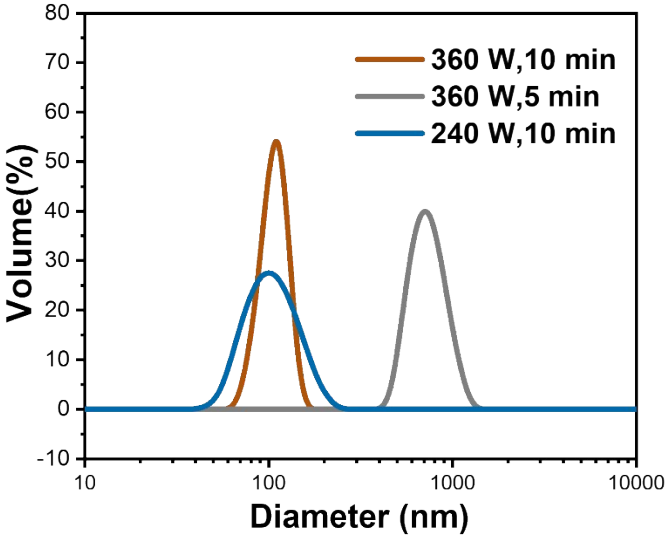

Fig. S1. Size distribution of PLGA nanoparticles prepared under different ultrasonication intensity and duration.

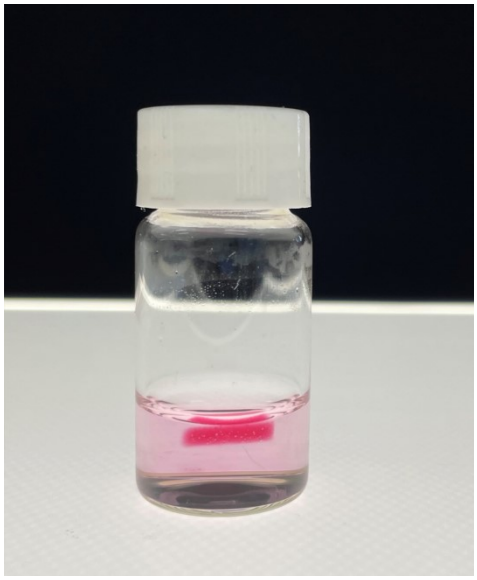

Fig. S2. The photograph of calcium cross-linked alginate hydrogel loaded with VB_{12} (pink) and NGF.

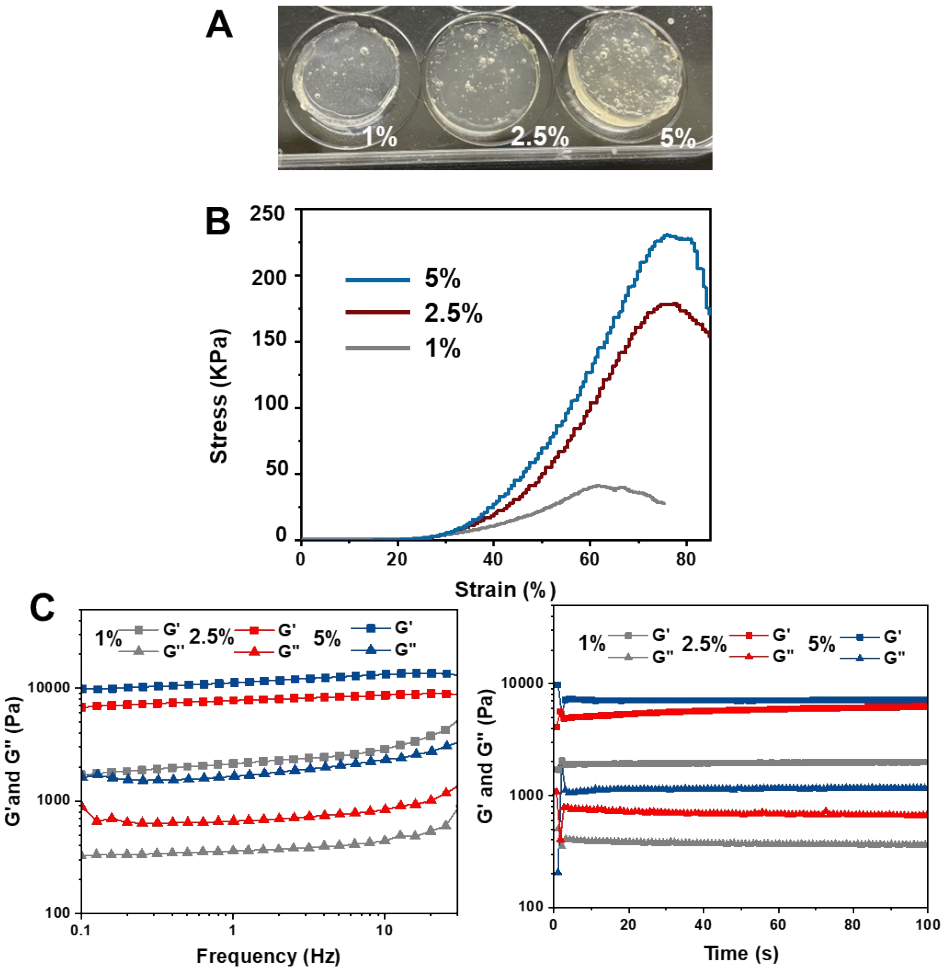

Fig. S3. (A) The photograph of calcium cross-linked alginate hydrogel with 1%, 2.5%, and 5% concentration of alginate. (B) The stress-strain curve of each concentration of hydrogel. (C) Rheological characterizations of alginate hydrogels with different concentration.

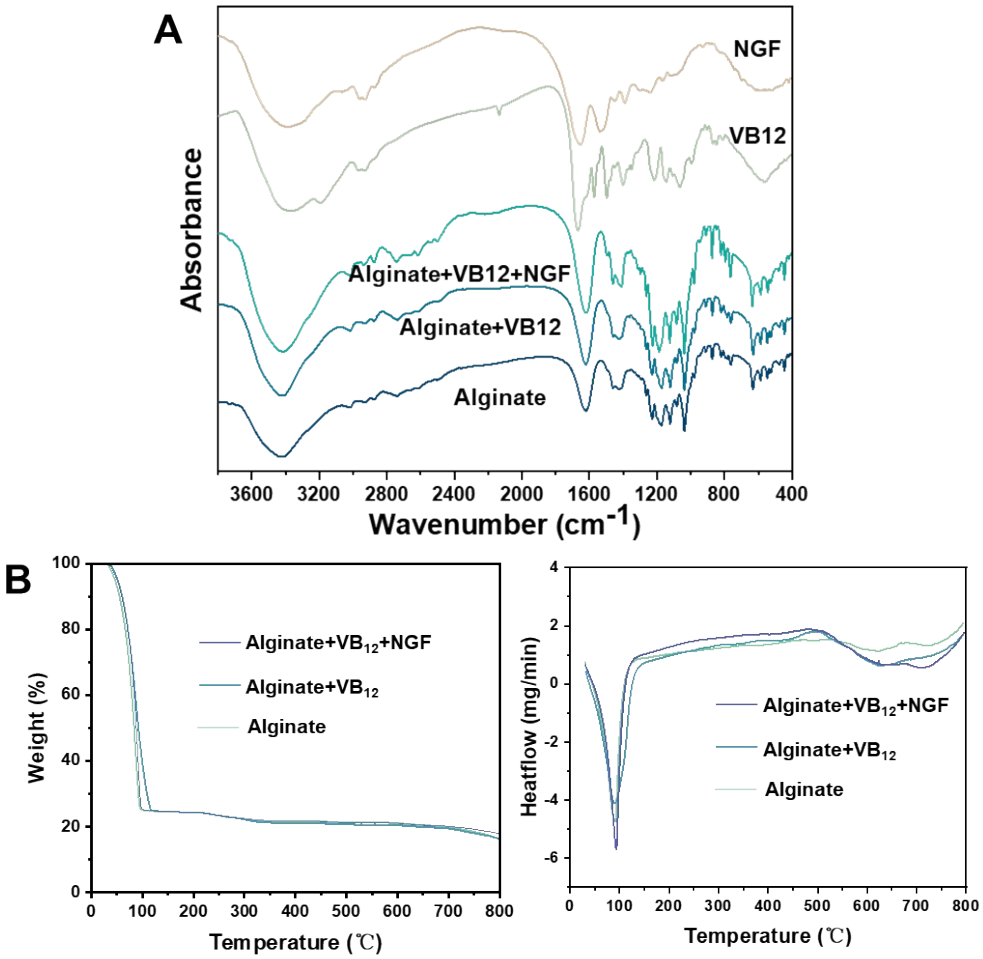

Fig. S4. A. The result of FTIR test of alginate, alginate + VB_{12}, alginate + VB_{12} +NGF, NGF and VB_{12}. B. TG-DSC test of alginate, alginate + VB_{12}, alginate + VB_{12} +NGF.

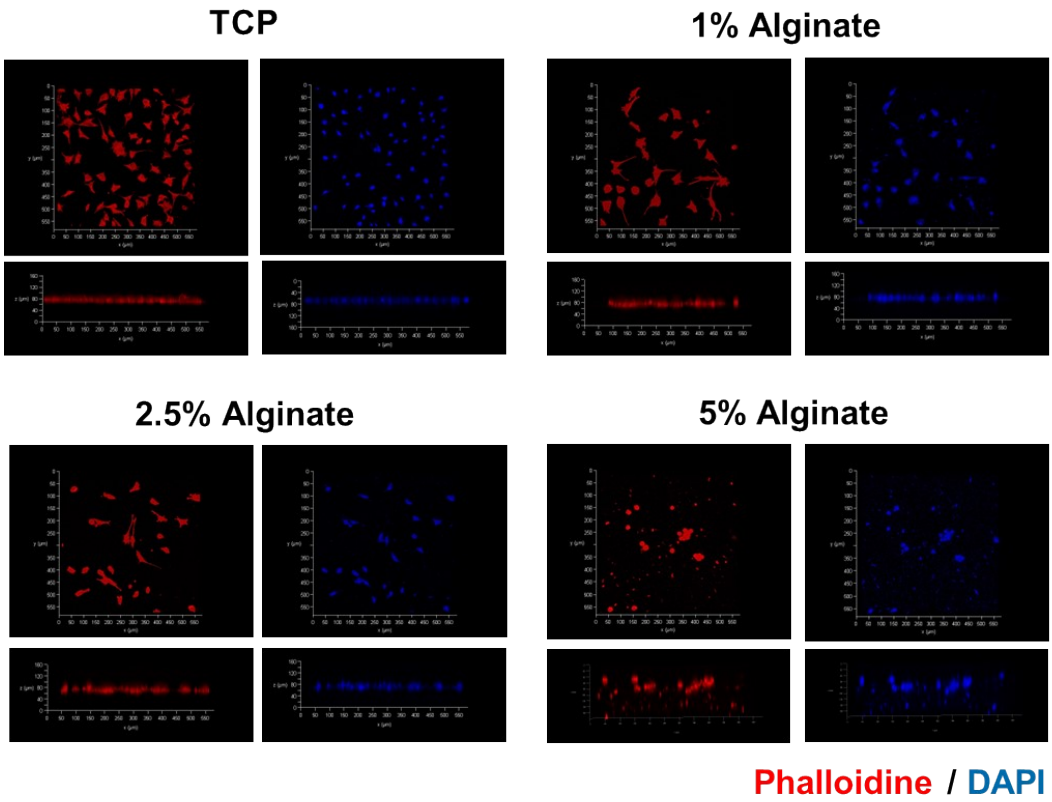

Fig. S5. Three-dimensional cytoskeleton (red) and DAPI (blue) staining photographs of PC12 cells cultured on TCP and UCDS with 1%, 2.5% and 5% concentration of hydrogel.

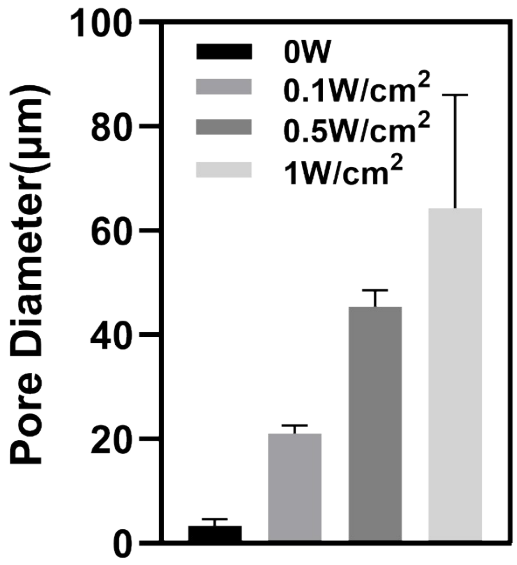

Fig. S6. Statistical data of the pore diameter of the ultrasound-responsive calcium cross-linked alginate hydrogel with no stimulation, 0.1W/cm^2, 0.5W/cm^2 and 1W/cm^2 intensity of stimulation.

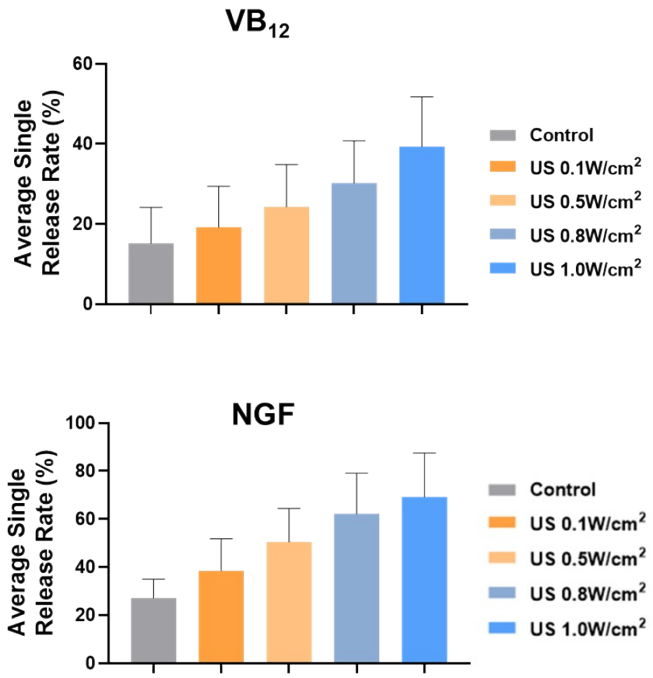

Fig. S7. The statistical data of the single release amount of VB_{12} and NGF in the first three days under different intensities of ultrasonic stimulation.

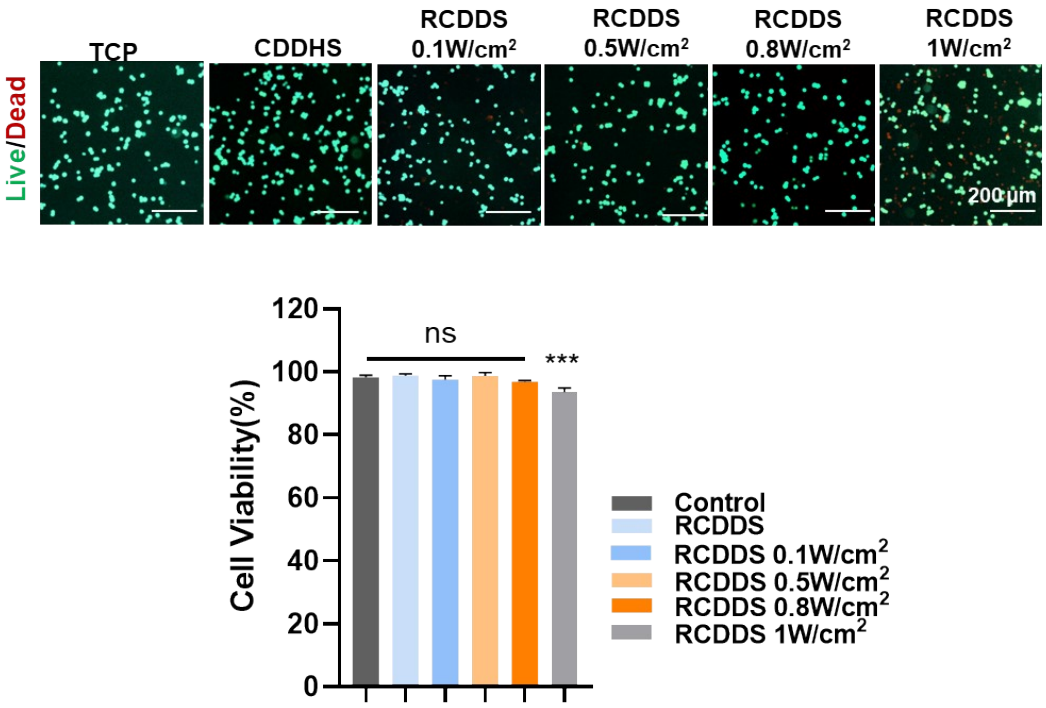

Fig. S8. Results of the representative photo and quantitative analysis of live/dead assay (n = 3) of different groups.

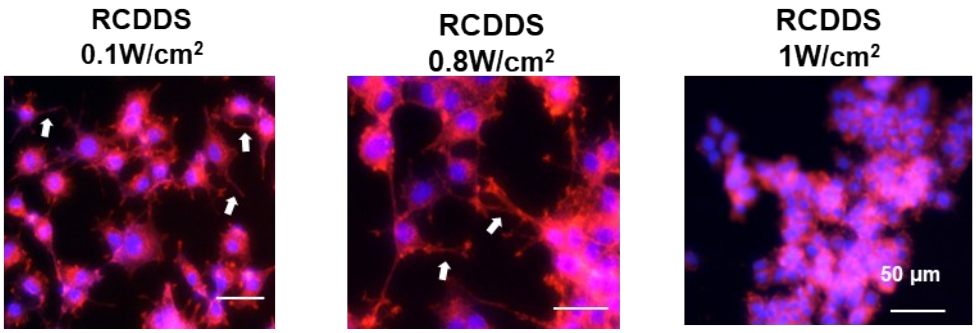

Fig. S9. Representative images of cytoskeleton staining of PC12 cells of RCDDS + 0.1W/cm^{2}US, RCDDS + 0.8W/cm^{2}US and RCDDS + 1W/cm^{2}US.

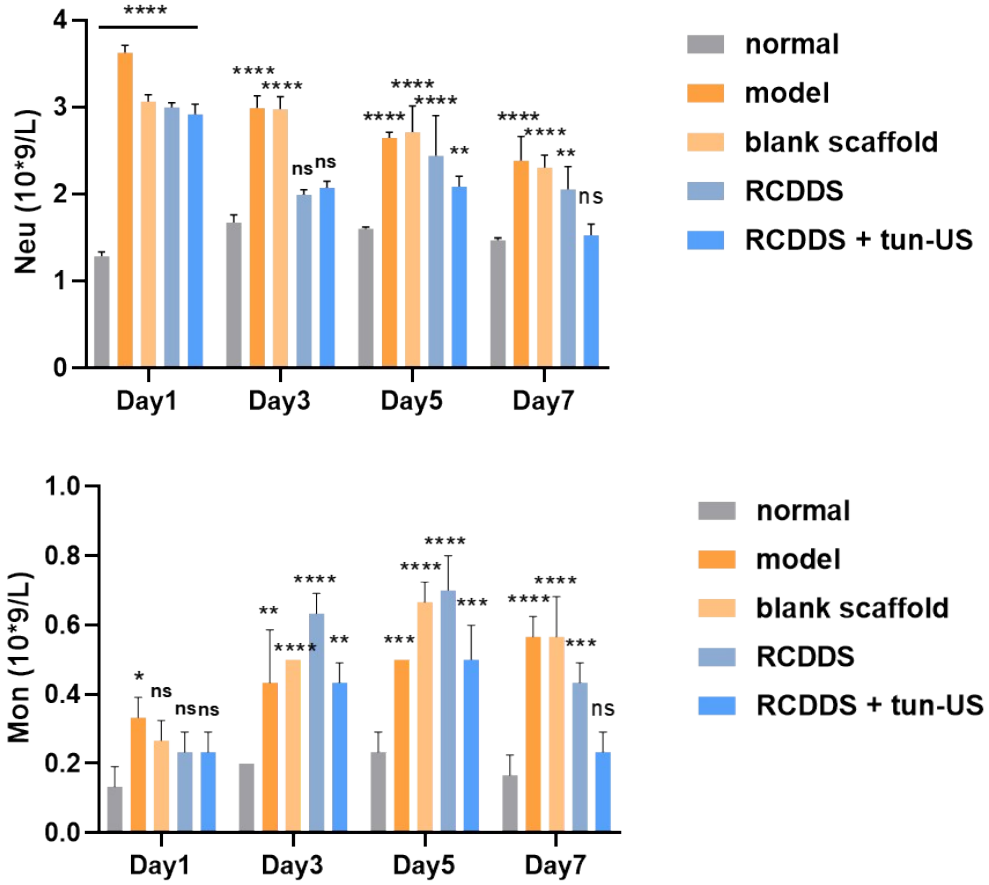

Fig. S10. Blood routine examination results of neutrophil and monocytes of the rats in five different groups (normal, model, blank scaffold, RCDDS and RCDDS + tun-US) at day1, 3, 5 and 7 after nerve injury (n = 3).

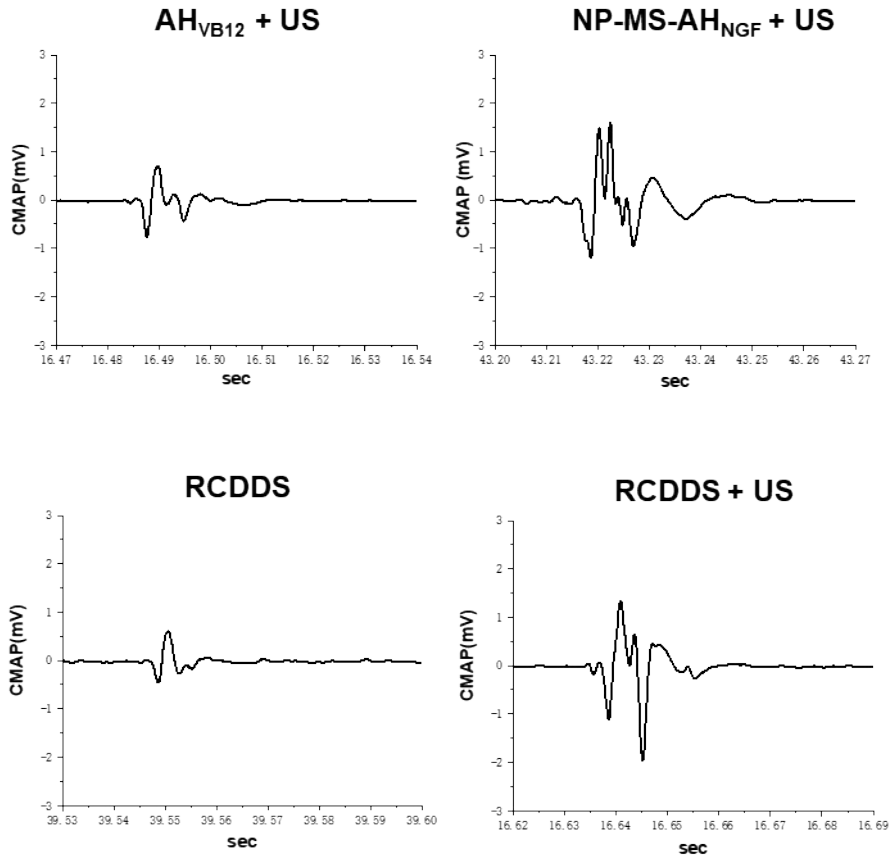

Fig. S11. Representative CMAP waveform of the rats from AH_{VB12} + US group and NP-MS-AH_{NGF} + US group, RCDDS groups and RCDDS + US group.