

CELL SURVIVAL DATA PROCESSING WITH ARTIFICIAL NEURAL NETWORKS

Kosterev V.V.*, Mishulina O.A., Trofimov A.G.

Moscow Engineering Physics Institute (State University), Moscow, Russia

Laboratory investigations of the hyperthermia effect on the malignant cells result in the assembly of experimental values of cell survival under different conditions for the same cell type. In most cases experimental data are represented as assembly of survival curves $z(t, T_k)$, $k = \overline{1, K}$, where t is the hyperthermia duration, T_k is the temperature and k is the experimental curve number. Each of these curves is based on limited number n_k experiments carried out at the hyperthermia durations t_i , $i = \overline{1, n_k}$, and fixed temperature T_k .

The available experimental data are usually noisy because of inaccuracy of biological experiment realization and the processing of its results. The other feature of experimental data consists in their incompleteness because of complexity of experiment performance. Therefore, the number of experimental points at the survival curves as well as the number of these curves usually is not great.

In this paper we pose the following problems:

- smoothing of the experimental data set $z(t_i, T_k)$, $i = \overline{1, n_k}$, $k = \overline{1, K}$;
- reconstruction of values $z(t^*, T_k)$ at the experimental curves obtained for the hyperthermia durations t^* that don't coincide with the experimental values t_i , $i = \overline{1, n_k}$;
- construction of survival curves $z(t, T^*)$ corresponding to the fixed temperatures T^* that don't coincide with the experimental values T_k , $k = \overline{1, K}$.

The feature of the problem posed consists in the absence of the mathematical model of cell survival and any a priori information about the mechanism of cell killing under hyperthermia. On basis of experimental data we develop the mathematical model of the function $z(t, T)$ which is capable to evaluate the cell survival fraction $z(t^*, T^*)$ at arbitrary point (t^*, T^*) . We propose to use the artificial neural networks [1, 2] to solve this problem.

We develop the special neural net architecture for cell survival $z(t, T)$ modeling. This neural network includes the recurrent neural net (*RNN*) module, which allows representing of cell survival function depending on t . The *RNN* parameters are controllable and depend on T . Thus, the developed neural model is referred to as *Controlled RNN – CRNN*. The structure scheme of *CRNN* is shown in Fig. 1. The neural approximation of function $z(t, T)$ denoted in Fig. 1 as $y(t, T)$ is observed at the output neuron *ON*. By adjusting the *RNN* parameters experimental curves $z(t, T)$ may be approximate by output variable $y(t, T)$. The multilayer neural network (*MNN*) is used for *RNN* parameters adjusting.

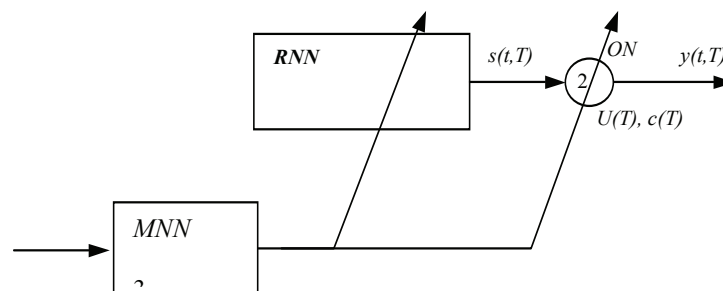


Fig. 1. Controlled recurrent neural net (CRNN) scheme

The special two-stage learning procedure was developed for the neural structure shown in Fig. 1. At the first stage the RNN and ON parameters are iteratively adjusted using the experimental data $\{z(t_i, T_k), i = \overline{1, n_k}\}$ that corresponds to the fixed temperatures $T_k, k = \overline{1, K}$. The learning is performed in accordance with the modified "back propagation through time" ($BPTT$) method [2, 3]. At the second stage we use the sets of RNN and ON parameters obtained at the first stage for MNN training. The MNN training is performed by means of back propagation method (BP) [2, 3].

The considered neural model with $N = 3$ recurrent neurons was constructed for Chinese hamster V79 cells survival data [4, p.19]. The set of the experimental curves corresponds to the cells survival data as the function of their duration time in a water bath at the different temperatures. The MNN with one hidden layer ($K = 4$ neurons) was applied to RNN parameters adjusting. The considered model was used for experimental data approximation and cells survival prognosis for arbitrary values t and T in working range. In Fig. 2 we present the curves, reconstructed by the trained neural model. The survival curve corresponding to the temperature $T^* = 43.5^\circ\text{C}$ was constructed by the neural model.

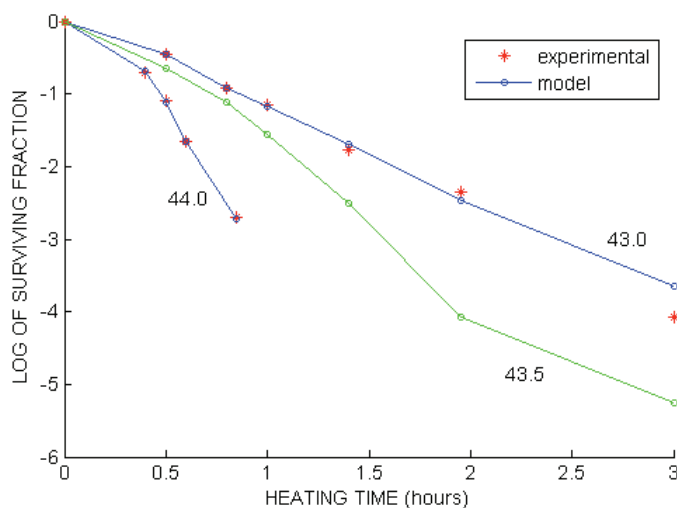


Fig. 2. Survival curves for Chinese hamster V79 cells constructed by $CRNN$ model for hyperthermia temperature $T^* = 43.5^\circ\text{C}$ lacking in experimental data. Survival curves corresponding to temperatures $T = 43.0^\circ\text{C}$ and $T = 44.0^\circ\text{C}$ are approximated using the neural model

Neural modeling of cell survival function $z(t, T)$ shows that the developed neural structure approximates the experimental data and forecasts cells survival fraction for the arbitrary temperature and heating time with satisfactory accuracy. It's possible to conclude that the developed neural structure may be perspective for cells survival modeling under more general experimental conditions including ionizing radiation, pH factor or hypoxia.

References

1. Kosterev V.V., Averkin A.N. A Framework for Fuzzy Model of Thermoradiotherapy Efficiency. 22nd Annual Meeting of the European Society for Hyperthermic Oncology. Abstract Book. Graz, Austria, June 08 – 11, 2005, p. 51-52.
2. Osowskii S. Neural Nets for Information Processing. Oficyna Wydawnicza PW, 2000, 344 pp.
3. Mishulina O. A., Kharitonov V. S. et al. Two Neural Network Models for Nuclear Engineering Applications. Optical Memory & Neural Networks, 4, 2005.
4. Hyperthermia and Oncology / ed. by M. Urano and E. Double. Vol. 2: Biology of Thermal Potentiation of Radiotherapy. – Zeist: VSP, 1989, 175 pp.

Supported by Project No 2221 of ISTC.