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Research Article

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Modeling and Simulation of Cancer Treatment Using Cold Atmospheric Plasma

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Abstract

The cold atmospheric plasma (CAP) becomes a promising technology for the cancer cell treatment. There are many aspects affecting the effect of the treatment including plasma discharge voltages, CAP exposure time, cancer cell type and so on. In order to have a further understanding the cancer treatment using CAP jet, we proposed a mathematical model by using the least square method for the response of cancer cell line of U-87 MG with CAP jets treatment based on experimental data from reference. The comparison demonstrates that the mathematical model can capture the characteristics of the cancer cell viability in the experimental data. It means that we can use the same method to predict cancer cell response to CAP under a nominal condition. We also proposed the mathematic model using the Taylor expansion method according to the processed data to study the correlation between the cell viability, the treatment and the CAP exposure time.

Keywords: CAP jet; cancer treatment; mathematic model

Background

CAP jets as the non-equilibrium plasma, have been studied for many years and developed as a new promising therapeutic technology in cancer treatment [1, 2, 3, 4]. As the CAP jets could just aim killing cancer cells without damaging the healthy ones [5, 6, 7, 8, 9, 10, 11], it has been successfully used in lung carcinoma treatment, breast cancer treatment, head and neck carcinoma treatment, neuroblastoma treatment and so on [12, 13, 14, 15, 16].

Kim et al applied the CAP jet for lung carcinoma treatment, demonstrating the effects of the CAP jet on the mouse lung carcinoma and fibroblast cells [17]. The CAP jet was applied in breast cancer treatment and the results showed that the CAP jets had a very sensitive effects on the breast cancer cells [18]. The plasma jet was investigated for the anti- cancer treatment, and the cell death effects of the CAP jet and its molecular mechanisms were studied using the N_2 and air plasma jets, demonstrating the potential employment of the CAP jets in the cancer therapy. It is found that CAP jets can be used to generate the oxygen species to initiate the cancer cell apoptosis [19].

Graves et al presented a simulating model to analyze the thermal effects of the target using the CAP jet dynamics, showing the importance of the feedback control on the achieving spatially uniform dose delivery [20, 21].

Researchers found that there are many plasma parameters affecting the cancer treatment including the applied voltage, temperature, properties of the target, cancer types, and plasma composition, and so on [12, 13, 15, 16]. What's more, it is found that the CAP exposure time has a crucial effect on the plasma characteristics and cancer cell viability [22].

In order to help further understanding the cancer treatment using CAP jet, we try to study the simulation method of the cancer treatment using CAP jets. In this paper, we processed the experimental data from reference [23], then proposed the mathematic model using the processed data to study the relation between the cell viability, CAP jets exposure time and the treatment time. We select the cell response of cancer cell line of U-87 MG under the CAP treatment. Firstly, we got the average viability according to the experimental data. Then use the least square method to get the coefficients of the mathematical model. Finally, we use the Taylor expansion method to get the polynomial of the cancer cell viability related to the CAP exposure duration and the CAP treatment time to predict the cancer cell viability under a nominal condition.

Results and Discussion

Here we have processed the experimental data from [23] in Tables 1 to 5, which show the cell viability over 0 to 48 h under CAP exposure durations of 0 s, 30 s, 60 s, 90 s, and 180 s, respectively.

Table 1: Dynamic response of cancer viability for U-87 with U=3.16 kV and CAP exposure time $\Delta t = 0\ s$

	Experiment 1	Experiment 2	Experiment 3	Experiment 4
0 h	0.9332	0.9332	0.9332	0.9332
0.4 h	2.5668	2.5668	2.5668	2.5668
0.8 h	4.0000	4.0000	4.0000	4.0000
1 h	3.5763	3.7744	4.0126	3.8137
6 h	4.4705	4.4705	5.0372	5.1706
12 h	5.0414	5.6080	5.3080	5.3414
24 h	5.6825	5.8159	5.4826	6.1492
48 h	5.7986	6.2986	6.1652	6.1986

Table 2: Dynamic response of cancer viability for U-87 with U=3.16 kV and CAP exposure time $\Delta t = 30\ s$

	Experiment 1	Experiment 2	Experiment 3	Experiment 4
0 h	0.4667	0.8167	0.5444	0.35
0.4 h	2.0220	2.2165	2.3720	2.4108
0.8 h	3.6548	4.0826	3.9660	3.8104
1 h	3.7325	3.9658	3.7710	4.2380
6 h	4.7784	4.7008	5.1674	4.8174
12 h	5.0463	5.4352	5.2796	5.2019
24 h	5.3870	5.8925	5.5814	6.5925
48 h	6.0681	6.0292	5.7959	6.6125

Table 3: Dynamic response of cancer viability for U-87 with U=3.16 kV and CAP exposure time $\Delta t = 60\ s$

	Experiment 1	Experiment 2	Experiment 3	Experiment 4
0 h	0.2333	0.4	0.2	0.3334
0.4 h	1.8667	1.7997	1.8333	1.7660
0.8 h	3.2662	3.6325	3.2661	3.1328
1 h	3.7327	3.9327	3.8993	3.9912
6 h	4.0960	4.2628	4.5626	4.5626
12 h	4.7919	5.0586	4.9586	5.2252
24 h	5.3172	5.9172	4.6172	5.1839
48 h	3.2013	4.3016	3.1346	3.8346

Table 4: Dynamic response of cancer viability for U-87 with U=3.16 kV and CAP exposure time $\Delta t = 90\ s$

	1	2	3	4
0 h	0.1955	0.19553	0.1995	0.2513
0.4 h	1.5083	1.4245	1.6480	1.3687
0.8 h	3.4916	3.5474	3.2681	3.1005
1 h	3.9324	3.8826	3.5195	3.8796
6 h	4.1894	4.4972	4.6089	4.5251
12 h	3.0726	2.9608	2.9888	2.7653
24 h	2.6536	2.8212	2.5139	2.5698
48 h	2.4581	2.5698	2.4022	2.2905

Table 5: Dynamic response of cancer viability for U-87 with U=3.16 kV and CAP exposure time $\Delta t = 180\ s$

	1	2	3	4
0 h	0.3351	0.3575	0.2011	0.2011
0.4 h	1.0502	0.8938	1.2960	1.1173
0.8 h	1.9888	1.7653	2.0782	1.9217
1 h	2.7932	2.5698	2.6815	2.4581
6 h	3.7318	3.8882	3.1955	3.0614
12 h	1.7877	1.8994	1.4301	1.2067
24 h	1.4078	1.4748	1.2201	1.1843

48 h	1.2737	1.3184	1.1620	0.9385

In order to investigate the cancer cell viability with time, we formulate a mathematical expression to cancer cell viability at different CAP exposure durations. Firstly, we got the average viability according to the tables 1 to 5, which is shown in Table 6.

Table 6: The Dynamic response of cancer viability for U-87 with U=3.16 kV with different CAP exposure times

	$\Delta t = 0s$	$\Delta t = 30s$	$\Delta t = 60s$	$\Delta t = 90s$	$\Delta t = 180s$
0 h	0.9332	0.5444	0.2916	0.2094	0.2737
0.4 h	2.5668	2.2553	1.8164	1.4874	1.0893
0.8 h	4.0000	3.8784	3.3244	3.3519	1.9385
1 h	3.7942	3.9268	3.8889	3.8035	2.6256
6 h	4.7872	4.8660	4.3710	4.4552	3.4692
12 h	5.3247	5.2407	5.0086	2.9468	1.5809
24 h	5.7825	5.8633	5.2588	2.6396	1.3217
48 h	6.1152	6.1264	3.6180	2.4302	1.1732

Based on the experimental results, we proposed an expression for the net proliferation rate *p*. (1)

$$p(\mathrm{t}) = (\mathrm{a}_1 + a_2\,\mathrm{t} + a_3\,\mathrm{t}^2)\exp(-a_4{}^{-t}) / (\mathrm{a}_5\mathrm{t}^2 + a_6) \qquad (1)$$

Where $a_1, a_2, a_3, a_4, a_5, a_6$ are the coefficients to be determined for each CAP exposure time by the data in Table 6. We use the least squares method to process the discrepancy between the mathematical model and data in Table 6 to get function expression for each exposure time. That means the coefficients of $a_1, a_2, a_3, a_4, a_5, a_6$ were got by solving the following objective function.

$$J = min\sum_{i=1}^{n}\int_0^{48}\|p_e(t) - p(t)\|^2 dt \qquad (2)$$

Combine Eq. (1) and (2), we obtain the coefficients of $a_1, a_2, a_3, a_4, a_5, a_6$ for each expression of cancer cell viability with CAP exposure time of 0s, 30 s, 60 s, 90 s, and 180 s, which can be seen in the following Table 7.

Table 7: The coefficients for the expression of cancer viability for U-87 with U=3.16 kV of different CAP exposure times

Δt	C_1	C_2	C_3	C_4	C_5	C_6
0 s	-2.138×10^{-6}	-5.373×10^{-6}	-7.353×10^{-6}	1.224	-1.267×10^{-6}	-5.723×10^{-7}
30 s	8.127	-35.13	180.6	165.6	32.24	4.413
60 s	10.73	34.72	60.49	58.22	13.73	13.35
90 s	24.58	340.5	43.29	2.785	21.88	51.23
180 s	6.027×10^{-6}	4.107×10^{-5}	1.281×10^{-6}	2.466	2.262×10^{-6}	1.033×10^{-5}

Figures 1 shows the comparison of the mathematical simulation results and the experimental data for U-87 MG with applied voltage of 3.16 kV at different CAP exposure time of 0 s, 30 s, 60 s, 90 s, and 180 s, respectively. It demonstrates that the mathematical model in this paper captures the experimental data successfully.

Figure 2 shows the dynamics response of cancer cell viability of the mathematical simulation model with plasma voltage of 3.16 kV for cancer cell of U-87 MG. From figure 2, we can get the cancer cell viability at any time for the five CAP exposure time with the voltage of 3.16 kV.

We can conclude from figure 1 and figure 2 that the mathematical model can be used to predict the cancer cell viability under any CAP treatment conditions. We can just combine the formula (1) and formula (2) and calculate the coefficients using the least square method.

In order to have a better understanding of the response of cancer cell viability of U-87 MG for arbitrary CAP exposure duration, we also investigate the correlation of the cancer cell viability with the CAP exposure time and the treatment time.

Then, we use the Taylor expansion method to get the polynomial of the cancer cell viability related to the CAP exposure duration and the CAP treatment in the following expression (3).

$$p(\Delta t, t) = a_0 + a_1 \Delta t + a_2 (\Delta t)^2 + a_3 \Delta t \cdot t + a_4 t^2 \qquad (3)$$

According to the data in Table 6, we obtain the coefficients

$$a_0 = 2.229, \quad a_1 = 0.02233, \quad a_2 = 0.56, \quad a_3 = -0.0005, \quad a_4 = -0.002$$

Figure 3 shows the response of the cancer cell viability from generalized mathematical model (3) for arbitrary CAP treatment duration Δt and time t. We can use formula (2) to predict the cancer cell viability for arbitrary CAP treatment duration Δt and time t. For example, $\Delta t = 25\,s$, t = 3 h, the cancer cell viability could be around 3.52.

Conclusions

CAP is a promising technology in the cancer cell treatment. The cancer cell viability under the CAP treatment is influenced by plasma discharge voltages, CAP exposure time, gas composition, cancer cell type and so on. In this paper, we proposed the mathematical simulation model to predict the cancer cell viability under arbitrary CAP exposure time and treatment time.

(1) We use the average cancer cell viability and the least square method to solve the coefficients of the proposed mathematical model. Then we compare the response of the cancer cell viability from the mathematical model and the experimental data, it is found that the mathematical model can capture the characteristics of the response successfully. It means that we can use the same method to predict cancer cell response to CAP under a nominal condition.

(2) We also proposed the mathematic model using the Taylor expansion method using the average data to study the correlation between the cell viability, CAP exposure time and the treatment time. We can use it to predict the cancer cell viability for arbitrary CAP treatment duration Δt and time t. That is to say the cancer cell viability can be predict using the same method to under any CAP treatment conditions.

Material and Method

We proposed the mathematic model using the experimental data in Ref [23]. We select the experimental data of cancer cell line of U-87 MG under the CAP treatment. The CAP exposure duration is from 0 s to 180 s and the applied voltage is 3.16kV. We proposed the mathematical model to study the relation between the cell viability, CAP jet exposure time and the treatment time.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests

Funding

Not applicable

Authors' contributions

Minghao Xu is the sole author of the article.

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Not applicable

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Figure legend

Figure 1: Comparison of the mathematical simulation results of cell viability with experimental data for U-87 MG with the applied voltage of 3.16 kV at different CAP exposure time of (a)$\Delta t = 0s$, (b) $\Delta t = 30s$, (c) $\Delta t = 60s$, (d) $\Delta t = 90s$, and (e) $\Delta t = 180s$

Figure 2: The mathematical simulation model with plasma voltage of 3.16 kV for cancer cell of U-87 MG.

Figure 3: Response of cell viability from generalized mathematical model (3) for arbitrary CAP treatment duration Δt and time t.

Figures

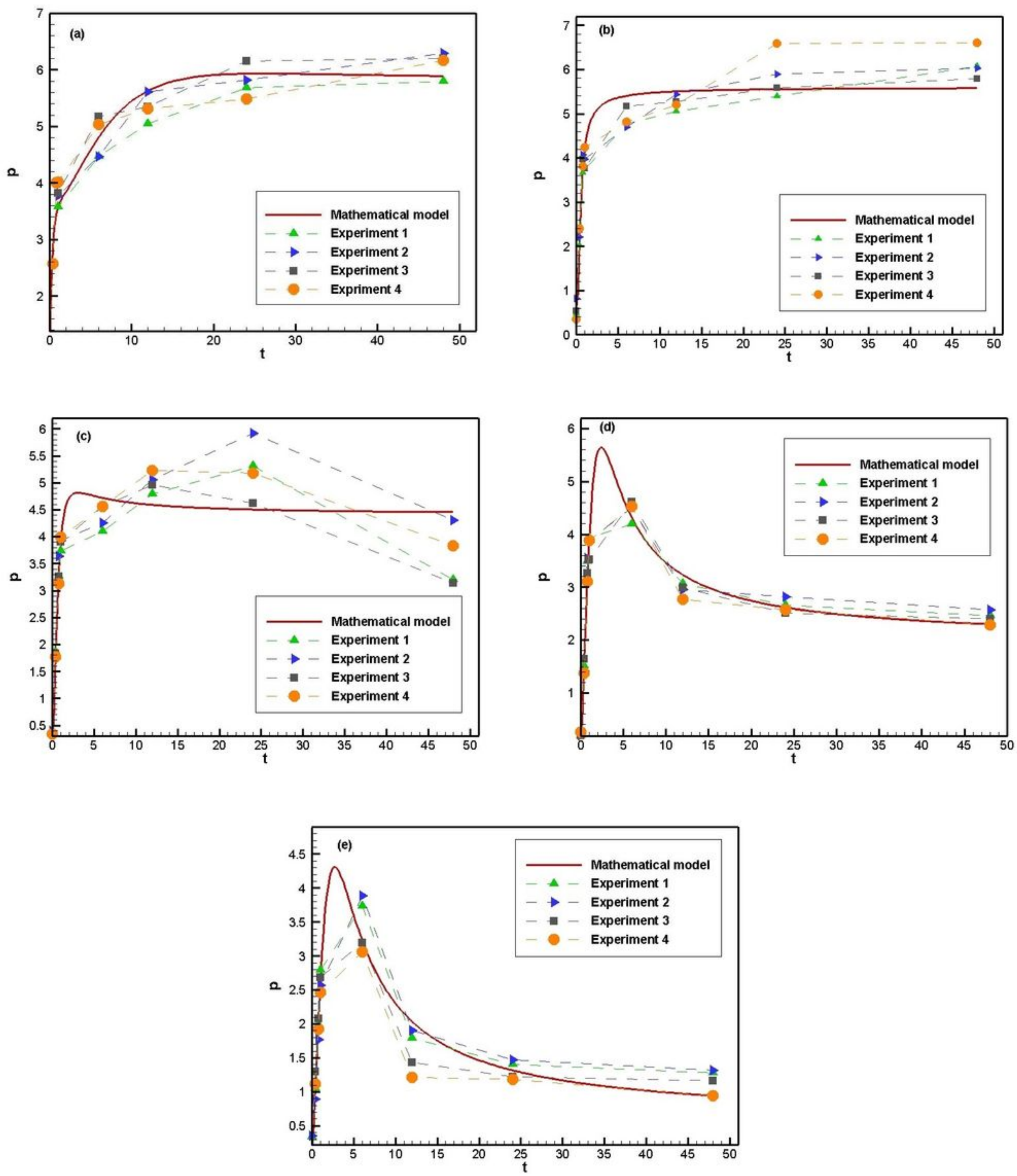

Figure 1

Comparison of the mathematical simulation results of cell viability with experimental data for U-87 MG with the applied voltage of 3.16 kV at different CAP exposure time of (a)Δt=0s, (b) Δt=30s, (c) Δt=60s, (d) Δt=90s, and (e) Δt=180s

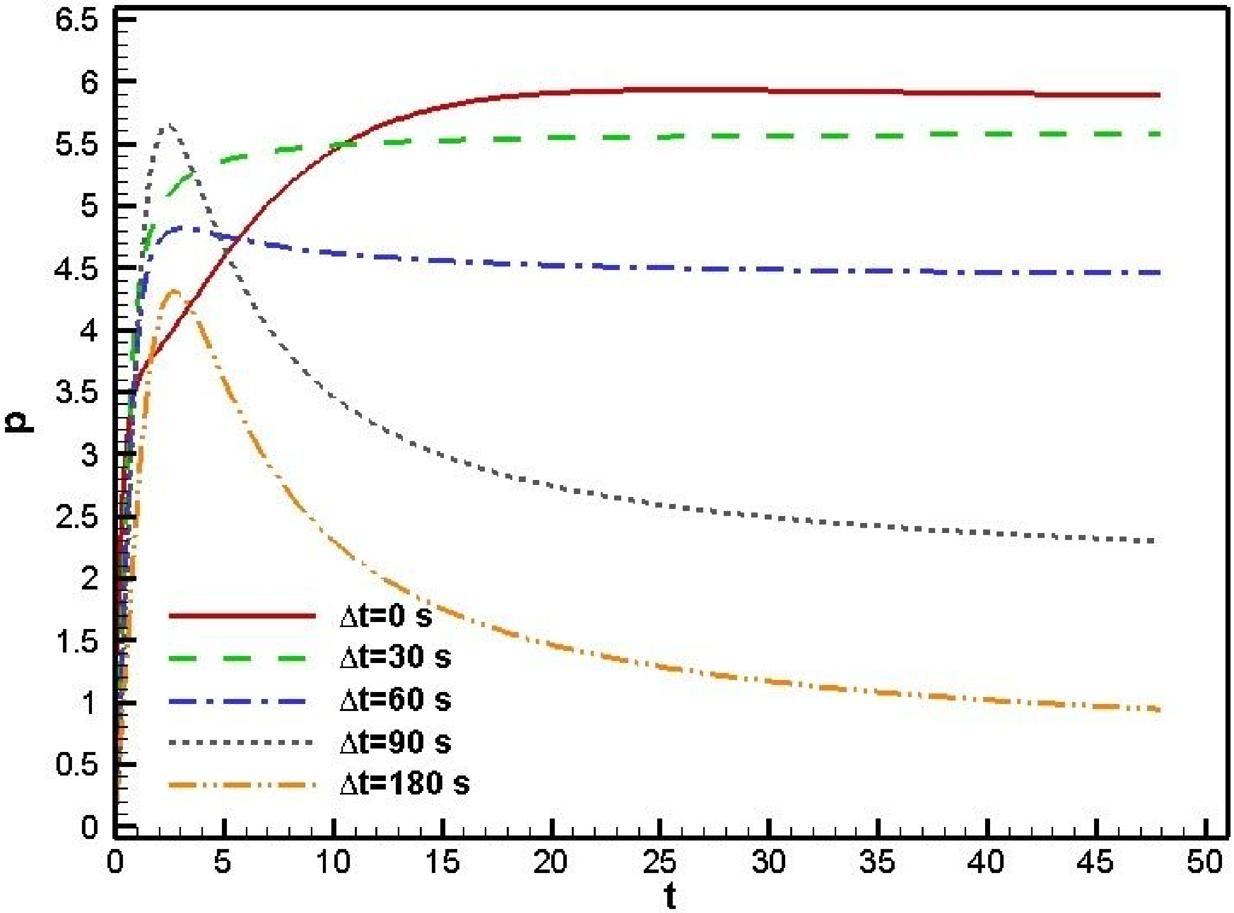

Figure 2

The mathematical simulation model with plasma voltage of 3.16 kV for cancer cell of U-87 MG.

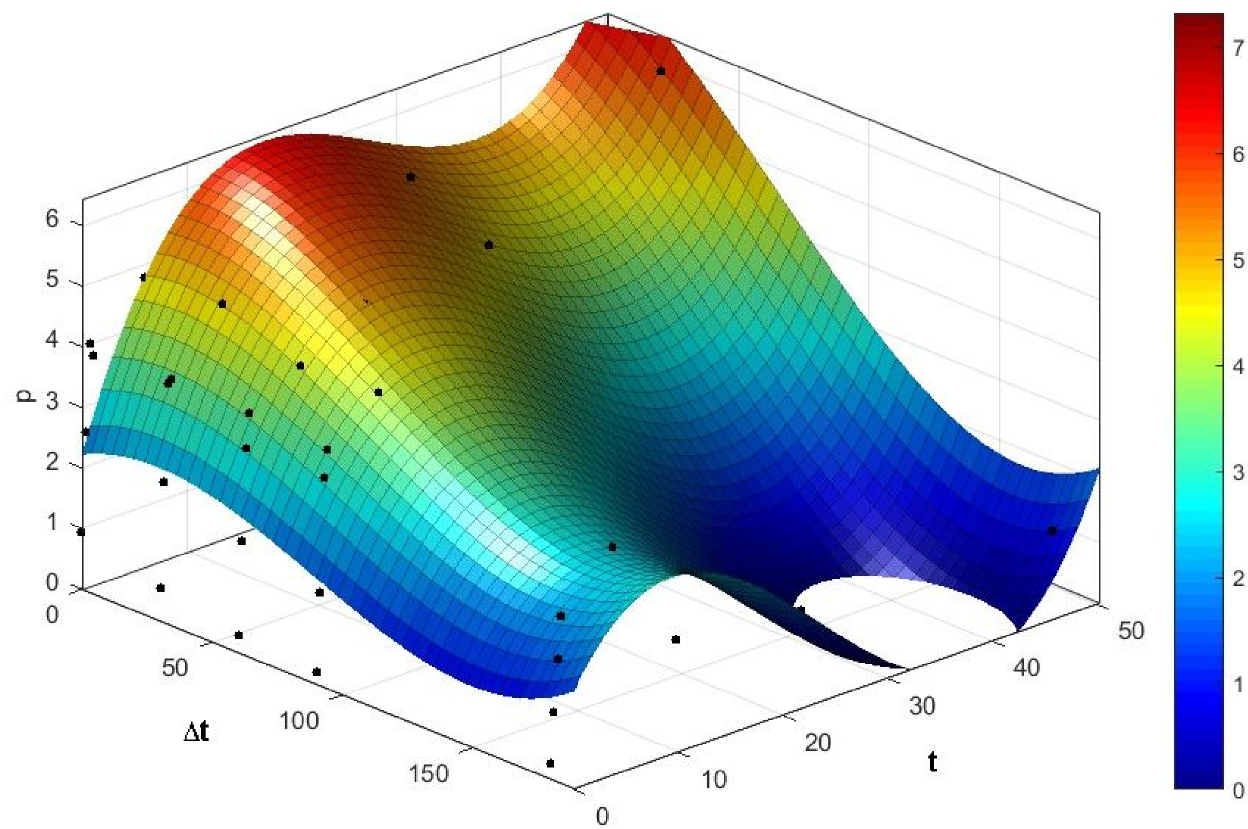

Figure 3

Response of cell viability from generalized mathematical model (3) for arbitrary CAP treatment duration Δt and time t.