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# KRIGING SURROGATE BASED OPTIMIZATION OF THERMAL DAMAGE TO LIVING BIOLOGICAL TISSUES BY LASER IRRADIATION BASED ON A GENERALIZED DUAL PHASE LAG MODEL

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## ABSTRACT

Large number of numerical computer simulations in engineering places is a serious burden on associated optimization problems nowadays. Kriging Surrogate based optimization (KSBO) becomes standard practice in analyzing expensive and time-consuming simulation. This paper aims to investigate the surrogate based analyze and optimization of thermal damage in living biological tissue by laser irradiation using a generalized duel phase model. The relationships of maximum temperature and thermal damage in living biological tissues of the response with two variables at a time are studied. The result shows that the surrogate model predicted response variables i.e., temperature and thermal damage are in good agreement with the original values. This result will help to predict the thermal damage and temperature of living tissue without solving the large numeric computer simulation rather using surrogate kriging model.

(1)

Keywords: Living tissue, thermal damage, Kriging Surrogate model

## 1. INTRODUCTION

Lasers are a very new piece of technology that has been presented in the medical field that contain many applications. With it first being introduced in the medical field in the 1960's in cardiovascular surgery it has made great strides in small and precise movements in surgery reducing the amount of human error. In the span of 5 decades, use of lasers has spanned for the treatment of eyes, kidneys, varicose veins and other parts of the body [Wang, X, et al. 2021, Sun, C., et al. 2021, Zhang, Q., et al. 2021].

The use of varieties of lasers in different types of surgeries often creates problems. There are many factors that need to be considered when it comes to the settings of lasers. Two important factors for the application of lasers are the pulse and intensity. These two setting can have a big impact on the depth that the laser will go into as well as the damage it will do to the biological tissue. The most concerning type of laser induced damage is the thermal damage that it has to the surrounding tissue when it performs surgery. As Pierce describes that the thermodynamic principles are the same in that there occurs "Observed irreversible thermal alterations range from substantial structural disruption due to steam evolution in high temperature short-term activations to low temperature rise, long-term initiation of the complex protein cascades that result in apoptosis and/or necroptosis."

First must be understood about the result of this laser induced thermal damage in biological tissue is that the veins as well as the surrounding tissue each vary in diameter depending on the area of the body. We must see the general bioheat equation considering blood perfusion and metabolic heat generation as it shows below [Pennes, H. H., 1948].

$$\rho c \frac{\partial T}{\partial t} = -\frac{\partial q}{\partial t} + Q_L + Q_m + w_b \rho_b c_b (T_b - T)$$

In the equation, q is heat flux,  $\rho$  and c are density and specific heat for the tissue.  $w_b$  is the blood perfusion rate and  $T_b$  and T are the temperatures of blood and tissue;  $Q_m$  and  $Q_L$  are the source term due to the metabolic heating and hyperthermia therapy.

From the general heat equation above, we have various constant and from them we can also assume that the vein temperature along with the tissue temperature to be the same. Something different however is that the blood perfusion rate was taken from various parts of the body in order to be able to calculate the laser damage and depth.

The simplest example of DPL model is its first order expansions for both q and T, given as [Tzou, D. Y., 1997]:

$$q(\mathbf{r},t) + \tau_q \frac{\partial q(\mathbf{r},t)}{\partial t} = -k \left[ \frac{\partial T(\mathbf{r},t)}{\partial x} + \tau_T \frac{\partial^2 T(\mathbf{r},t)}{\partial t \partial x} \right]$$
(2)

Combining the Eqs. (1) and (2), Jianhua [Zhou, J., et al. 2009] end up with this bioheat conduction equation with heat flux, q(x, t) and temperature T(x, t) that was used as a governing equation to simulate the DPL heat conduction in tissue:

$$\tau_{q} \frac{\partial^{2} q}{\partial t^{2}} + \frac{\partial q}{\partial t} = \alpha \frac{\partial^{2} q}{\partial x^{2}} + \alpha \tau_{T} \frac{\partial^{3} q}{\partial t \partial x^{2}} - \alpha \frac{\partial Q_{L}}{\partial x} + \alpha w_{b} \rho_{b} c_{b} \frac{\partial T}{\partial x} + \alpha w_{b} \rho_{b} c_{b} \frac{\partial T}{\partial x}$$
(3)

Considering not only interfacial convection heat transfer but also the blood perfusion, the two-step model can be written in the following forms:

$$\begin{split} \varepsilon \rho_b c_b [\frac{\partial T_b}{\partial t} + \vec{V} \cdot \nabla T_b] &= \varepsilon k_b \nabla^2 T_b + G(T_s - T_b) + \varepsilon Q_L \\ (1 - \varepsilon) \rho_s c_s \frac{\partial T_s}{\partial t} &= (1 - \varepsilon) k_s \nabla^2 T_s + G(T_b - T_s) + (1 - \varepsilon) Q_L + (1 - \varepsilon) Q_m \end{split}$$
(4)

where G is called lumped coupling factor between blood and tissue. G can be expressed as follows:

$$G = a_b h_b + w_b c_b \tag{6}$$

Combining Eqs. (1) and (5), while eliminating temperature T by operator method gives the following bioheat equation for heat flux:

$$\tau_q \frac{\partial^2 q}{\partial t^2} + \frac{\partial q}{\partial t} = \alpha_s \frac{\partial^2 q}{\partial x^2} + \alpha_s \tau_T \frac{\partial^3 q}{\partial t \partial x^2} - \alpha_s \frac{\partial s}{\partial x} - \frac{G}{(1-\varepsilon)\rho_s c_s} \left[ q + \tau_q \frac{\partial q}{\partial t} \right]$$
(7)

In this study, following equation will be used as the basic governing equation to make a similarity of the Eq. (3):

$$\tau_q \frac{\partial^2 q}{\partial t^2} + \frac{\partial q}{\partial t} = \alpha_s \frac{\partial^2 q}{\partial x^2} + \alpha_s \tau_T \frac{\partial^3 q}{\partial t \partial x^2} - \alpha_s \frac{\partial s}{\partial x} + \frac{G\alpha_s}{(1-\varepsilon)} \frac{\partial T}{\partial t} + \frac{G\alpha_s \tau_T}{(1-\varepsilon)} \frac{\partial^2 T}{\partial t \partial x}$$
(8)

For highly absorbed tissues, the surface laser heating is approximated as boundary condition of second kind. In this case the laser volumetric heat source or laser irradiance, QL is zero and the boundary conditions are given by [Zhang, Y., 2009, Afrin, N., et al. 2012] :

For, x=0, when 
$$0 < t < \tau_L$$
  
 $a = \phi_{in}(1 - R_d)$ 

For, x = L when  $0 < t < \tau_L$ , q = 0 (9)

For strongly scattering tissues, laser heating which is considered as body heat source is not equal to zero  $(Q_L \neq 0)$  and the irradiated surface is considered as thermally insulated. So, the boundary condition can be represented as:

For, x=0 when 
$$0 < t < \tau_L$$
  $q = 0$   
For, x= L when  $0 < t \tau_L$   $q = 0$   
(10)

And the initial conditions are:

At, t=0, q=0 and  $\frac{\partial q}{\partial t} = 0$  for 0<x<L (11) The laser volumetric heat source can be determined as follows:

The laser volumetric heat source can be determined as follows:  $Q_L(x) = \mu_a \phi(x)$  (12)

To calculate light distribution in scattering tissue broad beam laser method [Afrin, N., et al. 2012] is adopted and the light distribution can be determined by the following relation:

$$\phi(x) = \phi_{in}[C_1 \exp(-k_1 z/\delta) - C_2 \exp(-k_2 z/\delta)]$$
(13)  
The effective penetration depth can be defined by the diffusion theory as  
$$\delta = \frac{1}{\sqrt{3u_2[u_2+u_2(1-q)]}}$$
(14)

Here,  $\mu$ s is the scattering coefficient and g is the scattering anisotropy. The optical properties varied to represent the spectrum of tissues encountered in laser application are,  $0.1 \le \frac{\mu_s}{(\mu_a + \mu_s)} \le 0.999$  and  $0.7 \le g \le 0.9$  [Gardner, C., et al. 1996]. An improved scattering coefficient can be introduced as

 $\mu_s' = \mu_s(1-g)$  (15) As for the calculation of thermal damage ( $\Omega$ ), the Arrhenius integration is widely used, which is given as [Welch, A. J., 1994,Xu, F., et al. 2009]:  $\Omega = A \int_{-\infty}^{t_f} arr(-\frac{E}{2}) dt$  (16)

$$\Omega = A \int_{t_0}^{t_0} exp(-\frac{1}{RT}) dt$$
(16)

where A is the frequency factor, 3.1x1098 s-1 [Xu, F., et al. 2009]; E is the energy of activation of denaturation reaction, 6.28x105 J/mol [Xu, F., et al. 2009]; R is the universal gas constant, 8.314 J/ (mol K); T is the absolute temperature of the tissue at the location where thermal damage is calculated; t0 is the time at onset of laser exposure; and tf is the time of thermal damage evaluation. When  $\Omega$ =1.0, then the tissue is assumed irreversible damage which causes the denaturation of 63% of the molecules.

Performing integration of Eq. (8) over the control volume with grid point P in Fig.1 and over the time step from t to  $t+\Delta t$ :

$$\int_{w}^{e} \int_{t}^{t+\Delta t} (\tau_{q} \frac{\partial^{2} q}{\partial t^{2}} + \frac{\partial q}{\partial t}) dt dx = \int_{w}^{e} \int_{t}^{t+\Delta t} (\alpha_{s} \frac{\partial^{2} q}{\partial x^{2}} + \alpha_{s} \tau_{T} \frac{\partial^{3} q}{\partial t \partial x^{2}} - \alpha_{s} \frac{\partial Q_{L}}{\partial x} + \frac{G\alpha_{s} \tau_{T}}{(1-\varepsilon)} \frac{\partial^{2} T}{\partial t \partial x} dt dx$$

$$(17)$$

Appling backward difference in time and piecewise-linear profile in space, the following algebraic equation for temperature can be obtained from Eq. (17):

$$a_P q_E^{p+\Delta t} = a_E q_E^{t+\Delta t} + a_W q_W^{t+\Delta t} + b$$
(18)  
where,

(19)

$$a_E = \frac{\alpha_s \Delta t}{(\delta x)e} + \frac{\alpha_s \tau_T}{(\delta x)_e}$$

$$a_W = \frac{\alpha_s \Delta t}{(\delta x)_w} + \frac{\alpha_s \tau_T}{(\delta x)_w}$$
(20)

$$a_P = a_w + a_e + \frac{\tau_q \Delta x}{\Delta t} + \Delta x \tag{21}$$

$$b = \left[\frac{2\tau_q \Delta x}{\Delta t} + \Delta x + \frac{\alpha_s \tau_T}{(\delta x)_e} + \frac{\alpha_s \tau_T}{(\delta x)_w}\right] q_P^t - \frac{\alpha_s \tau_T}{(\delta x)_e} q_e^t - \frac{\alpha_s \tau_T}{(\delta x)_w} q_w^t - \frac{\tau_q \Delta x}{\Delta t} q_P^{t-\Delta t} - \alpha_s \mu_a \Delta x \Delta t \frac{\partial \phi}{\partial x}\Big|_P + \frac{G\alpha_s}{(1-\varepsilon)} \frac{T_E^{t+\Delta t} - T_W^{t+\Delta t}}{2} - \frac{T_E^{t-T_W^t}}{2}\right]$$
(22)

In the Eq. (22), the value of  $\frac{\partial \phi}{\partial x}$  can be obtained from the Eq. (13).

#### 2. Kriging Surrogate method

Kriging also known as Gaussian process regression is a method of interpolation based on the Gaussian Process [Bufia, E. A., Cinnella, P., 2015]. Kriging method is a response surface model which represents a relationship between design variables and objective functions using stochastic process. Kriging equations are determined by fitting line through points to minimize weighted sum of squares between points and line. These equations are weighted based on spatial is autocorrelation, which determined from the semivariograms. Semivariogram measures the strength of statistical correlation as a function of distance.

Semi-variogram = 0.5×average [(value at location i-value at location j)2]  

$$\gamma(h) = \sum_{i=0}^{n} \frac{\{z(x_i) - z(x_i+h)\}^2}{2\pi}$$
(23)

Kriging method has both a deterministic and probabilistic component where both are the function of distance.

$$Z(s) = \mu(s) + \varepsilon'(s) + \varepsilon''(s)$$
(24)

The Kriging model has gained popularity for aerodynamics design which drastically reduce computational time required for objective function evaluation in the uncertainty quantification process. Kriging methods are basically used in aerodynamics design problem optimization. The model predicts the value if unknown point using stochastic processes where sample points are interpolated with Gaussian random function to estimate the trend of the stochastic process [Bufia, E. A., Cinnella, P., 2015, J.P.C., 2009, Joeng, S., et al. 2005, Park, K., et al. 2006, Jouhaud, J.-C, et al. 2005, Sommanawat, W., Kanok-Nukulchai, W., 2009].

Surrogate based optimization (SBO) is an optimization process where the original objective is replaced by iterative re-optimization and updating the analytically tractable and computationally cheap surrogate. It has been suggested for the design with time-consuming computational model. When high-fidelity model consumes time and becoming computationally expensive, the surrogate modeling which is constructed data from high-fidelity models provides faster approximations of the objectives and constraints at new design points to make sensitivity and optimization studies feasible [Lee, H., et al. 2016, Gel, A., et al. 2013, Wenzel, C., et al 2015]. The initial functional surrogate can be generated using high -fidelity model data obtained through sampling of design. Design of experiments involves the use of strategies for allocating samples within the design space. Figure 1 shows the model construction flowchart for a functional surrogate model. Nazia et al. applied surrogate based analysis to optimize thermal damage in living biological tissue by laser irradiation. They applied Latin Hypercube Sampling (LHS) and Response Surface Model (RSM) to study optimization of thermal damage. They found out that the input variables had quadratic response to maximum temperature and thermal damage of living tissue [Afrin, N., Zhang, Y., 2019]

Regression is a type of supervised machine learning that is used to predict continuous response. The major steps to speed up computations are import data, select data to train the model by selecting accurate model and use the model to predict new set of data. Regression analysis is a reliable method of identifying which variables have impact on the topic of interest. Frontiers in Heat and Mass Transfer (FHMT), 18, 46 (2022) DOI: 10.5098/hmt.18.46

#### 3. Results and discussions

Thermophysical properties of tissues [Yamada, Y., et al. 1995]:  $\rho$ =1000 kg/m3, k = 0.628 W/ (m K), c = 4187 J/(kg K); thermo-physical properties of blood vessel:  $\rho_b = 1060 \text{ kg/m3}$ ,  $c_b = 3860 \text{ J/(kg K)}$ ,  $w_b =$  $1.87 \times 10-3$  m<sup>3</sup>/ (m<sup>3</sup> tissue s): optical properties [23]:  $\mu_s = 120.0$  cm<sup>-1</sup>,  $\mu_a = 0.4$  cm-1, g = 0.9 ; blood temperature: T<sub>b</sub> = 37°C; metabolic heat generation:  $Q_m = 1.19 \times 10^3$  W/m<sup>3</sup> [Yamada, Y., et al. 1995]. The thickness of the slab of tissue is L = 5 cm, and the initial temperature is  $T_0 = 37^{\circ}C$ . The diffuse reflectance  $R_d = 0.05$  is used for the laser light distribution of scattering tissue. Two laser irradiances are considered,  $\phi_{in}\!\!=2$  W/cm² and 30 W/cm². The laser duration time  $\tau_L$  is 5s. After the model convergence test, a total of 120 grid points and a time step ( $\Delta t$ ) of 0.001s are employed. Three different values of the coupling factor are taken based on the blood perfusion rate. According to the blood perfusion rate w<sub>b</sub>=  $1.87 \times 10^{-3}$  m<sup>3</sup>/ (m<sup>3</sup> tissue s), the values of  $\varepsilon$  are 0.0079, 0.025 and 0.0845 [7] and the coupling factors are 67435, 55078 and 47488 W/m<sup>3</sup>K [Zhang, Y., 2009, Yamada, Y., et al. 1995, Glenn, T. N., Ganong W. F.,].



Figure 1: Regression Learner flowchart for the problem

To find out the surrogate model to observe temperature of the tissue and thermal damage, the paper used "Regression Learner" app in Matlab. The flow chart of the app in figure 1 shows a common workflow for the regression model in the Regression learner app. The regression learner is a train regression model to predict data using supervised machine learning. We choose cross validation option to use good estimate of the predictive accuracy of the final model trained using full data set. We trained all available nonoptimizable model types such as Linear Regression models (Interactions Linear, Robust Linear and Stepwise Linear), Regression Trees (Fine Tree, Medium Tree and Coarse Tree), Regression models (Linear SVM, Quadratic SVM, Cubic SVM, Fine Gaussian SVM, Medium Gaussian SVM and Coarse Gaussian SVM) and Gaussian Process Regression models (Rational Quadratic, square exponential, Matern 5/2 and Exponential). The result shows that for the Gaussian process regression model Matern 5/2 gave the minimum Root Mean Square Error (RMSE) value for 100 number of data points. RMSE represents model performance and fitness against the data. The lower the error the better the fitness. In this case, the Gaussian regression showed RMSE value of 2.7288. The prediction plot for Gaussian regression represents how well of this model makes prediction for the actual value. A perfect regression model has a predicted response is equal to true response means all the points lie in the diagonal line and the vertical line from the point to the diagonal line represent the error of the prediction of that point. Figure 3 shows the predicted vs actual value plot for the tissue temperature with respect to laser pulse and blood perfusion. Most of the actual value lies close to the prediction (diagonal line) which implies a good fit of the predicted function with the actual values.



Figure 2: Response plot for Tissue Temperature(K) vs laser  $pulse(\mu s)$  and blood perfusion (wb) with 100 data points



Figure 3: Predicted vs actual plot for the tissue temperature with independent variables laser pulse and wb

Figure 4 shows residual plot for tissue temperature(K) with true response with independent variables laser pulse and blood perfusion respectively. The difference between the observed value of the dependent variable and the predicted value is called the residual and each data point has one residual. The fig. 4 shows that the residual plot is random means the line is a good fit for the data.

Figure 5 shows the estimated and observed minimum MSE at different iteration (Optimizable GPR of the model). Optimizable model corresponding Gaussian regression model is enabled and the optimizable GPR model is used iterate through all the combination of hyperparameter for GPR model. The visualization (fig:5) shows that the error decreases as different combination of hyperparameters are validated. The first attempt to observe the optimization refers that we should consider more data points to get more accurate surrogate model to predict the new set of data. PCA can also be used to reduced dimensionality. After using regression model to predict data, one can use generated Matlab code which can use to train the model with new data. The advantages of generating code are training on huge data set, examine the code to learn how to train models and modify the code for further analysis. The generate code shows to process the data into the right shape, train a model and specify all model options, perform cross-validation, compute statistics and compute validation predictions and scores.



Figure 4: Residual plot for tissue temperature with true response



**Figure 5:** Estimated and observed minimum MSE at different iteration (Optimizable GPR of the model)



Figure 6: Comparison between Kriging method and numerical simulation values for tissue temperature

The advantage of Matlab regression learner app is that it will allow to export the best surrogate model which validates the optimization and then trained model can be used to make predictions using new data. To justify the surrogate model is valid or not, we used the best kriging



Figure 7: Response plot for tissue temperature optimization for 200 data points

exported model to predict new set of data which will validate the kriging

method. Supplied data inputs (laser pulse and blood perfusion) will

provide new set of data using the best kriging model by using "predictFcn

(input variables)". Figure 6 shows the comparison between the predict

data set from the best model and numerical simulation results. The figure

shows a good agreement with those data sets. The minimum RMSE value for thermal damage is 0.000188887 for Boosted Trees. The training time

for the method is 0.27933 second. Mean Squared Error (MSE) value is



Figure 8: Predicted vs actual plot for tissue temperature with independent variables (laser pulse)



**Figure 9:** Residual plot for tissue temperature with true response for 200 data points



Figure 10: Comparison between Kriging method and numerical simulation values for tissue temperature



Figure 11: Response plot for thermal damage optimization for 200 data points



Figure 12: Predicted vs actual plot for thermal damage with independent variables (laser pulse and blood perfusion) with 200 data points



Figure 13: Residual plot for thermal damage with true response

We increased number of data points up to 200 to consider temperature and thermal damage optimization as the results indicated that more data points would provide more accurate optimization of surrogate model. After training regression model in Regression Learner app in Matlab, we compared models based on model statistics, visualize results in the response plot, actual plot verses predicted plot, and by residual plot. Figure 7 shows the response plot for tissue temperature for 200 data points. Figures 8 shows predicted vs actual plot for tissue temperature with independent variables. It implies the effect of the model and compares the model against the null model. Most of the actual values for tissue temperature lies or close to the predicted curve which indicates a good fit of the model.

Figure 9 shows the residual plot for tissue temperature with true response for 200data points. Surrogate model can be evaluated by using residuals plot. Usually a good model has residual scattered roughly symmetrically around 0. Our result shows a good model since residuals are almost symmetrically distributed around 0 and residuals doesn't change significantly in size from left to right in the plot. Figure 10 shows the comparison between kriging method and numerical simulation values for tissue temperature. Figure 11 shows response plot for thermal damage optimization for 200 data points. Gaussian Process regression model Matern 5/2 GPR gave the lowest RMSE value 4.0989. Figure 12 shows the predicted plot vs true response plot for thermal damage. This figure helps to check the model performance. A perfect regression model has a predicted response the same as the observed values so all the points lies on the diagonal line. The data points are closed to be as close to the diagonal line and scattered roughly symmetrically around the line meaning the model can be improved. Boosted trees model type is used to train the data points to make it more flexible. Figure 13 shows the residuals plot vs true response. Figure 14 shows the comparison between the numerical simulation results and kriging model optimization results for thermal damage in living tissue. The figure indicates a good agreement with numerical and optimization results. Since the data points are not very large, cross-validation is used to validate the points which helps partition data into some number of folds, trains the model and calculate the average test error over all folds. In this paper the numerical solution is used to train the surrogate model. Figures 6 and 10 are the representation in terms of comparison of the training data and validation data. It shows from both of the figs that the numerical solution successfully train the surrogate model.

Overall from this study we can conclude that the Kriging surrogate model shows a good optimization model to predict the temperature and thermal damage of living tissue.



Figure 14: Comparison between Kriging method and numerical simulation values for thermal damage for 200 data points

## 3. CONCLUSIONS

The surrogate based analyze and optimization of thermal damage in living biological tissue is carried out for laser irradiation using a generalized duel phase model. The relationships of maximum temperature and thermal damage in living biological tissues optimization with independent variables blood perfusion and laser pulse are studied. The result shows that the surrogate model predicted response variables i.e, maximum temperature and thermal damage are in good agreement with the numerical result. This result implies that surrogate kriging model is sufficient to predict the thermal damage and temperature of living tissue, rather than the numerical simulation of full biological model.

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#### NOMENCLATURE

- *a* specific heat transfer area,  $m^2/m^3$
- c specific heat, J/ (kg K)
- G coupling factor between blood and tissue, W/(m3 K)
- t time, s
- T average temperature, K
- q heat flux vector,  $W/m^2$
- x position vector, m
- w blood perfusion rate, m3/m3 tissue
- $Q_L$  heat source due to hyperthermia therapy,  $W/m^3$
- $Q_m$  source terms due to metabolic heating,  $W/m^3$
- Rd diffuse reflectance of light
- A frequency factor,  $s^{-1}$
- R universal gas constant, J/(mol K)
- *E* energy of activation of denaturation reaction, *J/mol*

## Greek Symbols

- ρ density, kg/m3
- $\beta$  vector of unknown constant coefficients
- $\tau_q$  phase lag time of the heat flux, s
- $\tau_T$  phase lag of the temperature gradient, s
- $\tau_L$  laser exposure time, s
- *a* thermal diffusivity, m<sup>2</sup>/s
- $\varepsilon$  porosity
- $\phi$  in incident laser irradiance

## **Appendix: Exported model:**

function[trainedModel,validationRMSE]=trainRegressionModel(trainin gData) [trainedModel, validationRMSE] = trainRegressionModel(T) yfit = trainedModel.predictFcn(T2)inputTable = trainingData; predictorNames = { 'Tpulse', 'WB' }; predictors = inputTable(:, predictorNames); response = inputTable.Damage; isCategoricalPredictor = [false, false]; % Train a regression model % This code specifies all the model options and trains the model. regressionTree = fitrtree(predictors, response,'MinLeafSize', 4. 'Surrogate', 'off'); % Create the result struct with predict function predictorExtractionFcn = @(t) t(:, predictorNames);treePredictFcn = @(x) predict(regressionTree, x); trainedModel.predictFcn=@(x)treePredictFcn(predictorExtractionFcn(x)); % Add additional fields to the result struct trainedModel.RequiredVariables = {'Tpulse', 'WB'}; trainedModel.RegressionTree = regressionTree; trainedModel.About = 'This struct is a trained model exported from Regression Learner R2020b.'; trainedModel.HowToPredict = sprintf('To make predictions on a new table, T, use:  $\$  yfit = c.predictFcn(T) \nreplacing "c" with the name of the variable that is this struct, e.g. "trainedModel". \n \nThe table, T, must contain the variables returned by: \n c.RequiredVariables \nVariable formats (e.g. matrix/vector, datatype) must match the original training data. \nAdditional variables are ignored. \n \nFor more information, see <a href="matlab:helpview(fullfile(docroot, "stats", "stats.map"). "appregression\_exportmodeltoworkspace")">How to predict using an exported model</a>.');

- % Extract predictors and response
- inputTable = trainingData;
- predictorNames = {'laservPulse', 'wb'};
- predictors = inputTable(:, predictorNames);
- response = inputTable.Temp;
- isCategoricalPredictor = [false, false];
- % Perform cross-validation

partitionedModel = crossval(trainedModel.RegressionTree, 'KFold', 5); % Compute validation predictions

validationPredictions = kfoldPredict(partitionedModel);

% Compute validation RMSE

validationRMSE = sqrt(kfoldLoss(partitionedModel, 'LossFun', 'mse'));

# REFERENCES

Afrin, N., Zhou, J., Zhang, Y., Tzou, D. Y., Chen, J. K., 2012, "Numerical Simulation of Thermal Damage to Living Biological Tissue Induced by Laser Irradiation Based on a Generalized Duel Phase Lag Model", *Numerical heat transfer*, **61** A, 483-501.

## https://doi.org/10.1080/10407782.2012.667648

Afrin, N., Zhang, Y., 2019, "Surrogate-based Optimization of Thermal Damage to Living Biological Tissues by Laser Irradiation", *Frontiers in Heat and Mass Transfer*, **12**, 27.

# https://doi.org/10.5098/hmt.12.27

Bufia, E. A., Cinnella, P., 2015, "Efficient Uncertainty Quantification of Turbulent Flows Through Supersonic ORC Nozzle Blades", *Energy Procedia* **82**, *186–193*.

# https://doi.org/10.1016/j.egypro.2015.12.018

Gardner, C. M., Jacques, S. L., and Welch, A. J., 1996, "Light Transport in Tissue: Accurate, Heuristic for One-Dimensional Fluence Rate and Frontiers in Heat and Mass Transfer (FHMT), 18, 46 (2022) DOI: 10.5098/hmt.18.46

Escape Function Based Upon Monte Carlo Simulations", *Lasers in Surgery and Medicine*, **18**, *129–138*.

https://doi.org/10.1002/(SICI)1096-9101(1996)18:2<129::AID-LSM2>3.0.CO;2-U

Ganong W. F., Review of Medical Physiology, Eighteenth Edition, 537.

Gel, A., Garg, R., Tong, C., Shahnam, M., Guenther, C., 2013, "Applying Uncertainty Quantification to Multiphase Flow Computational Fluid Dynamics", *Powder Technology* **242**, 27-39.

https://doi.org/10.1016/j.powtec.2013.01.045

Glenn, T. N., *Rastegar,S., Jacques, S. L.*, 1996, "Finite Element Analysis of Temperature Controlled Coagulation in Laser Irradiated Tissue", *IEEE Transactions on Biomedical Eng.*, **43** (1), 79–87.

https://doi.org/10.1117/12.182958

J. P. C., 2009, "Kriging Metamodeling in Simulation: A Review", *European Journal of Operational research* **192**, 707-716.

https://doi.org/10.1016/j.ejor.2007.10.013

Jeong, S., Murayama, M., Yamamoto, K., 2005, "Efficient Optimization Design Method Using Kriging Model", *Journal of Aircraft*, **42** (2), 413-420.

https://doi.org/10.2514/1.6386

Jouhaud, J.-C., Sagaut, P., Labeyrie, B., 2005, "A Kriging Approach for CFD/Wind-Tunnel Data Companion", *Journal of Fluids Engineering* **128** (4), 847-855.

https://doi.org/10.1115/1.2201642

Lee, H., Jo, Y., Lee, D.-J., Choi, S., 2016, "Surrogate Model-based Design Optimization of Multiple Wing Sails Considering Flow Interaction Effect", *Ocean Engineering* **121**, 422-436.

https://doi.org/10.1016/j.oceaneng.2016.05.051

Park, K., Oh, P.-K., Lim, H.-J., 2006, "The Application of The CFD and Kriging Method to an Optimization of Heat Sink", *International Journal of Heat and Mass Transfer*, **49** (19-20), 3439-3447.

https://doi.org/10.1016/j.ijheatmasstransfer.2006.03.009

Pennes, H. H., 1948, "Analysis of Tissue and Arterial Blood Temperatures in the Resting Forearm", J. Appl. Physiol, 1 93–122.

https://doi.org/10.1152/jappl.1948.1.2.93

Sommanawat, W., Kanok-Nukulchai, W., 2009, "Multiscale Simulation Based on Kriging Based Finite Element Method", *Interaction and Multiscale Mechanics*, **2** (4), 353-374.

https://doi.org/10.12989/imm.2009.2.4.353

Sun, C., Ji, C., Li, Y., Kuang, J., Wu, J., 2021, "A Comparison Study of Photothermal Effect Between Moxibustion Therapy and Laser Irradiation on Biological Tissue", *International Journal of Thermal Science*, **164** 106924

https://doi.org/10.1016/j.ijthermalsci.2021.106924

Tzou, D. Y., 1997, Macro to Microscale Heat Transfer: The Lagging Behavior, Taylor & Francis, Washington, D.C..

Welch, A. J., 1984, "The Thermal Response of Laser Irradiated Tissue", *IEEE J. of Quantum Electronics*, **20**, *12*, *1471–1481*.

Wang, X., Qi, H., Yang, X., Xu, H., 2021, "Analysis of the Time-space Fractional Bioheat Transfer Equation for Biological Tissues During Laser Irradiation", *International Journal of Heat and Mass Transfer*, **177** *121555* 

https://doi.org/10.1016/j.ijheatmasstransfer.2021.121555

Wenzel, C., Otto, S., Prechtl, S., Parczyk, K., Steigemann, P., 2015 "A Novel 3D High-content Assay Identifies Compounds that Prevent Fibroblast Invasion into Tissue Surrogates", *Experimental Cell Research* **339** (1) 35-43.

https://doi.org/10.1016/j.yexcr.2015.10.003

Xu, F., Lu, T. J., Seffen, K. A., Ng, E. Y. K., 2009, "Mathematical Modeling of Skin Bioheat Transfer", *ASME Applied Mechanics Reviews* **62**, 050801.

https://doi.org/10.1115/1.3124646

Yamada, Y., Tien, T., Ohla, M., 1995, "Theoretical Analysis of Temperature Variation of Biological Tissues Irradiated by Light", ASME=JSME Thermal Engineering Conference, 4, 575–581.

https://doi.org/10.1016/j.csite.2021.100853

Zhang, Y., 2009, "Generalized Dual-phase Lag Bioheat Equations Based on Nonequilibrium Heat Transfer in Living Biological Tissues", *Int. J. Heat and Mass Transfer*, **52**, 4829–4834.

https://doi.org/10.1016/j.ijheatmasstransfer.2009.06.007

Zhang, Q., Sun, Y., Yang, J., Soh, A. K., Wang, X., 2021, "Theoretical Analysis of Thermal Response in Biological Skin Tissue Subjected to Multiple Laser Beams", *Case Studies in Thermal Engineering*, 24 100853.

https://doi.org/10.1016/j.csite.2021.100853

Zhou, J., Chen, J. K., and Zhang, Y., 2009, "Dual Phase Lag Effects on Thermal Damage to Biological Tissues Caused by Laser Irradiation", *Computers in Biology and Medicine*, **39**, 286–293.

https://doi.org/10.1016/j.compbiomed.2009.01.002