

## SUPPORTING INFORMATION–Training the Model

When training a model for binary classification, the goal is typically to learn a function  $f \cdot$  that can be used to predict the label for a new example. In our problem, the goal is to accurately predict a newly admitted patient's probability of testing positive for *C. difficile* during the current admission. Let  $\mathbf{x}_i$  represent the  $i^{\text{th}}$  training example, (i.e., patient admission).  $\mathbf{x}_i$  is a  $d$ -dimensional feature vector that is in  $[0, 1]^d$ . Let  $\mathcal{X}$  represent the feature space that  $\mathbf{x}_i$  lies in. Let  $y_i$  represent a binary label indicating whether or not the  $i^{\text{th}}$  patient tested positive for *C. difficile* during the current admission. Then our learning task is defined as follows:

$\mathcal{D} = \{(\mathbf{x}_i, y_i) \mid \mathbf{x}_i \in \mathcal{X}, y_i \in \{-1, 1\}\}_{i=1}^n$ , where  $n$  is the number of unique patient admissions available for training. In general, with logistic regression, we seek a function  $f: \mathbb{R}^d \rightarrow [0, 1]$  of the form:

$$f(\mathbf{x}_i) = \frac{1}{1 + e^{-b_0 + \mathbf{w}^T \mathbf{x}_i}}$$

where  $\mathbf{w} \in \mathbb{R}^d$  (and  $\mathbf{x} \in \mathbb{R}^d$ ). Solving for the regression coefficients  $\mathbf{w}$  and the offset  $b_0$  is a maximum likelihood estimation problem. When  $d$  is large, i.e., the data lie in a high-dimensional space, it is easy to overfit. Therefore, to improve generalizability to unseen future patient cases, and reduce the likelihood of overfitting to the training data, we employ L2-regularized logistic regression.<sup>18</sup> In L2-regularized logistic regression, a regularization term  $\frac{1}{2} \|\mathbf{w}\|^2$  is included in the objective function.

$$\min_{\mathbf{w}} \frac{1}{2} \|\mathbf{w}\|^2 + C \sum_{i=1}^n \log(1 + \exp^{-y_i \mathbf{w}^T \mathbf{x}_i}) \quad (\text{Eq. 1})$$

$C$  is a scalar tuning parameter that controls the tradeoff between the number of errors on the training set and the complexity of the model. Note, we add an extra constant dimension to  $\mathbf{w}$  and compute the offset  $b_0$  implicitly. The solution to Eq. 1 depends on the  $\{ \mathbf{x}_i, y_i \}_{i=1}^n$  employed in the training. The training data is used in Eq. 1 to find the optimal setting of  $\mathbf{w}$ . The hyperparameter  $C$  in Eq. 1 was found using five-fold cross-validation on the training set, sweeping the value from  $2^{-8}$  to  $2^{-1}$ .

## SUPPORTING INFORMATION–Calculating Colonization Pressure

In terms of *C. difficile*, colonization pressure (*CP*) aims to measure the number of infected patients, in a unit or hospital. In our analysis, the contribution a patient,  $p$ , makes to the *CP* on day,  $CPP(t)$ , depends on when the patient tested positive for the first and last time,  $t_f$  and  $t_l$ , and when the patient is discharged from the hospital  $t_d$  (where time is measured in days from the day of admission). While the patient continues to test positive he or she contributes a constant amount to the *CP*. After the last positive test result (which is often the first positive test result, since testing for a cure is not recommended) a patient contributes to the *CP* for no more than 14 days. During this time period, the patient is assumed to be treated or in isolation, and we assume a linearly decreasing relationship.

Equation 1 defines this function.

$$CPP_{p,t} = \begin{cases} 1 & t \in [t_f, t_l] \\ -\frac{t}{14} + \frac{(t_l+14)}{14} & t \in [t_l, \min t_d, t_l + 14] \\ 0 & otherwise \end{cases} \quad \text{Eq.1}$$

We have time-stamped locations for each patient, thus we calculate a colonization pressure for each unit,  $CPU_{u,t}$ , as in Equation 2. The  $CPU_{u,t}$  depends on each patient's contribution to the colonization pressure on that day and each patient's length of stay in unit,  $u$ , on day  $t$ ,  $LOS(u,p,t)$

$$CPU_{u,t} = \sum_p CPP_{p,t} * \frac{LOS(u,p,t)}{24} \quad \text{Eq.}$$

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When extracting the relevant **unit-wide colonization pressure** for a new patient on a given day we sum the  $CPU_{u,t}$  across all units in which that patient spent any time. As a result, the unit-wide colonization pressure varies across patients

for a given day. The **hospital-wide colonization pressure** is calculated as

${}_u CPU(u, t)$ , and is the same across all patients on a given day.