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SVM-based Drug Administration Decision Support System (DADSS)

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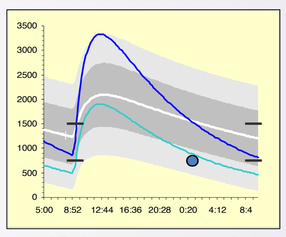
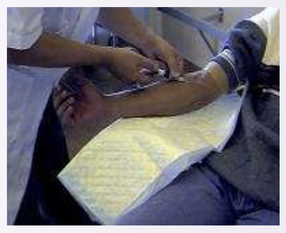
Introduction and Motivations

Current Practice

Analysis



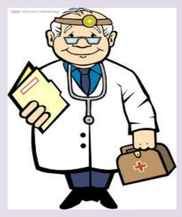
Build Concentration Curve using the Measured Value



Blood Sampling

Slow
Expensive
Invasive

Predicted trough drug concentration



Clinical Decision

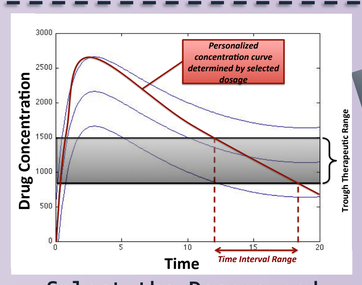
Recommended drug dosage and time interval

Weight
Dosage
…

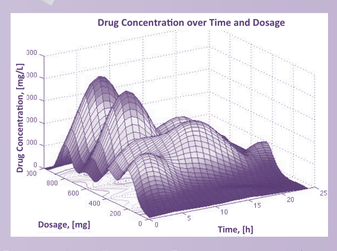
Patient

Patient profile
Physical measurements
External parameters
…

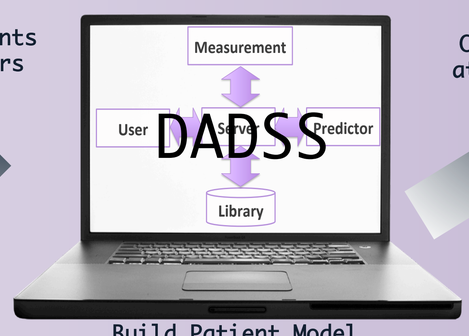
Our Approach



Select the Dosage and Time according to Therapeutic Range



Compute Drug Concentrations at different Time and Dosage



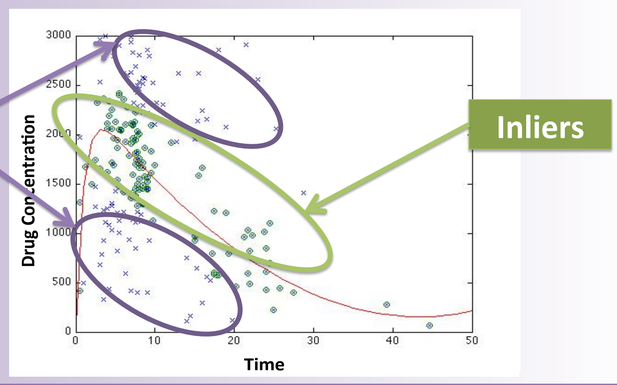
Build Patient Model

Fast
Less expensive
Not invasive
More accurate
More features

RANdom Sample Consensus (RANSAC)

- Used to separate efficiently inliers and outliers from data samples (remove noise);
- Estimate parameters for a potential model using basis functions:

$$\{x^{-2}, x, x^3, \log(x), \cos(x), (1-\exp(-x)), \exp(x)\}$$



Implementation

Library | **New Patient**

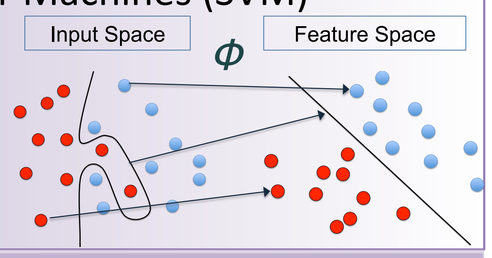
Preprocessing (Data completion, filtering, normalization)

Core (SVM-based Drug Concentration Prediction)

Selection (Drug's Dosage and Time Interval)

Support Vector Machines (SVM)

- Easy to understand;
- Able to process a large number of features;
- Deal properly with overfitting problem.



Features

Patient Profile

- *Individual Features*
  - Age, gender, weight, height, etc.
- *Clinical Features*
  - Diabetes, heart disease, cancer, etc.
- *Genomic features*
  - Family disease history.

Physical Measurements

- *Vascular Features*
  - Blood sugar, cholesterol level, pH value, etc.
- *Physical Features*
  - Blood pressure, heart rate, renal function, respiration frequency, respiration rhythm, respiration deepness, etc.

External Parameters

- *Symptom Features*
  - Vomiting, fever, dizziness, headache, convulsion, somnolence, shock, etc.
- *Habitual Features*
  - Amount of water, milk, smoke, alcohol, tea, coffee, sports, type of food, etc.
- *Environmental Features*
  - Humidity, temperature, etc.

Prediction Accuracy Using DADSS

Table 1 Sample Comparisons of Drug Concentration Predictions [1], [2] and DADSS methods. (Drug: *Imatinib*)

Drug Concentration Prediction [mg/L]	Measured	[1]	[2]	*DADSS*	%[1]	%[2]
Sample 1	1681.00	2455.80	1842.12	***1756.52***	+90.25%	+11.05%
Sample 2	1901.00	1383.10	1803.03	***1843.07***	+88.81%	+7.73%
Sample 3	1116.00	1639.20	1517.42	***1257.18***	+73.02%	+49.74%
Sample 4	2107.00	3296.60	2619.34	***2069.70***	+96.86%	+39.93%
Sample 5	1399.00	1732.80	3178.94	***1364.16***	+92.56%	+525.79%
Prediction Differences: ΔMEAN	-	667.86	590.56	***69.35***	**+89.62%**	**+78.04%**
Prediction Differences: ΔSTD	-	331.16	686.22	***43.43***	**+86.89%**	**+194.10%**
					Prediction Enhancement $\{\frac{DADSS-[1]}{[1]}, \frac{(DADSS-[2])}{[1]}\} \times 100\%$	

DADSS Recommendation Rules

- Users predefine the therapeutic ranges of peak and/or trough concentration values of a certain drug.
- In this patient example, we choose dosage to be 600mg and the time interval to be 12h after dosing. (Drug: *Imatinib*)

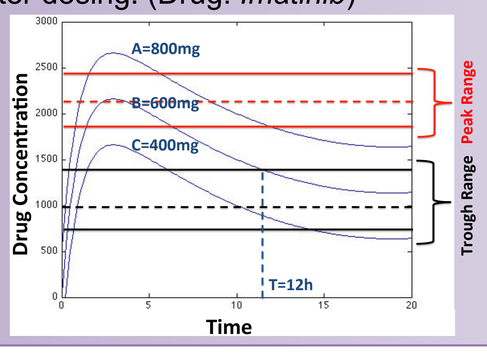


Table 2 Sample Recommendations From DADSS. M: Male, F: Female, G: Gastrointestinal stromal tumors. (Drug: *Imatinib*)

Patient Features					Recommendations	
No.	Gender	Age	Body Weight (Kg)	Disease	Dosage (mg)	Time (h)
1	M	82	56	G	400	13
2	F	58	53	G	500	15
3	F	62	54	G	700	16
4	M	58	100	G	800	18
5	M	47	73	G	500	14

- Given more features, DADSS can provide more personalized recommendations to patients and clinicians.

Publications:

- W. You, N. Widmer, and G. De Micheli, "Example-based Support Vector Machine for Drug Concentration Analysis", 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2011), pp. 153-157.
- W. You, N. Widmer, and G. De Micheli, "Personalized Modeling for Drug Concentration Prediction Using Support Vector Machine", 4th International Conference on Biomedical Engineering and Informatics (BMEI 2011), pp.1523-1527.

Under Review:

- W. You, A. Simalatsar, N. Widmer and G. De Micheli, "SVM-based Drug Administration Decision Support System", 34thAnnual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2012).
- W. You, A. Simalatsar, and G. De Micheli, "RANSAC-based Enhancement in Drug Concentration Predictions Using Support Vector Machine", International Workshop on Innovative Simulation for Healthcare (I-WISH 2012).

Future Work

- Evaluate the system performance using more data samples.
- Implement the system into mobile devices, e.g. iPhone and test the system on various drugs.
- Integration of the SVM-approach into a closed loop verification process of an autonomous drug delivery system.

References:

[1] D.W.A. Bourne, "Mathematical Modeling of Pharmacokinetic Data", 2nd ed. Technomic Publishing Company, Inc, 1995.
[2] W. You, N. Widmer, and G. De Micheli, "Example-based Support Vector Machine for Drug Concentration Analysis", 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2011), pp. 153-157.
[3] M. Fischler and R. Bolles, "Random Sample Consensus: A Paradigm for Model Fitting with Applications to Image Analysis and Automated Cartography", Communications of the ACM, vol. 24, no. 6, pp. 381-395, 1981.
[4] S.R. Gunn, "Support Vector Machines for Classification and Regression", Technical Report, University of Southampton.