Biomedical Time Series Representations in the Presence of Structured Information

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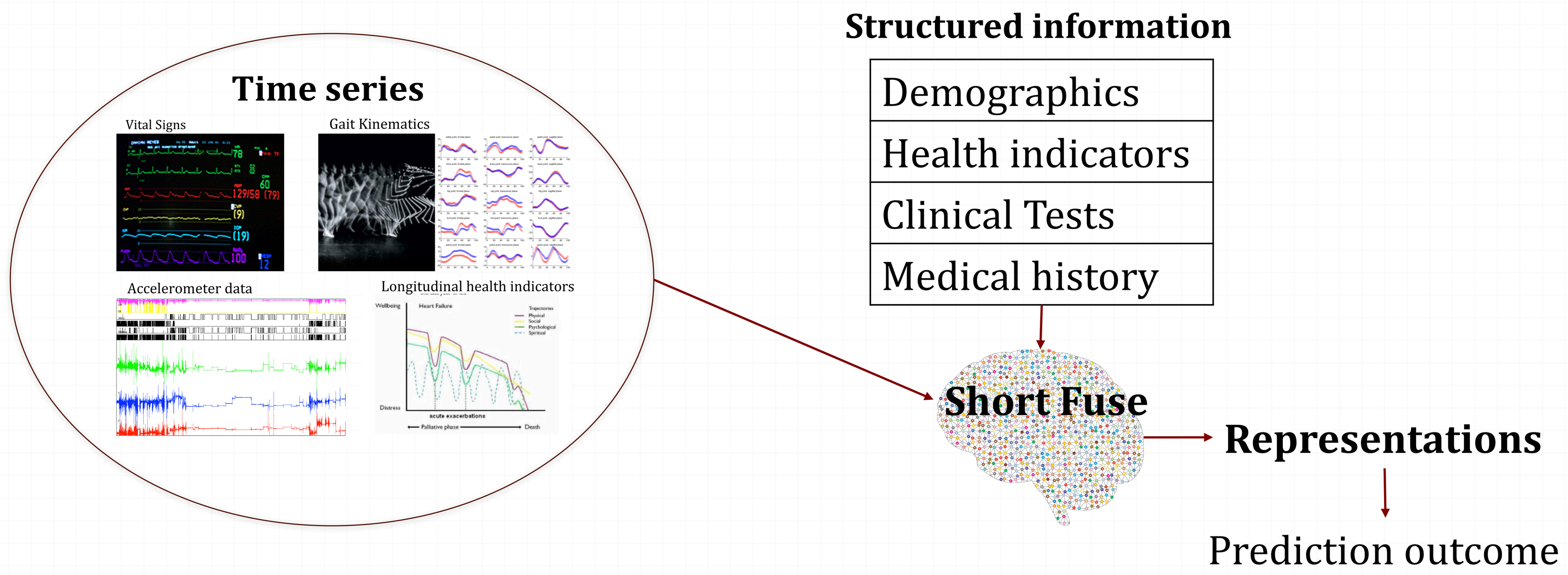
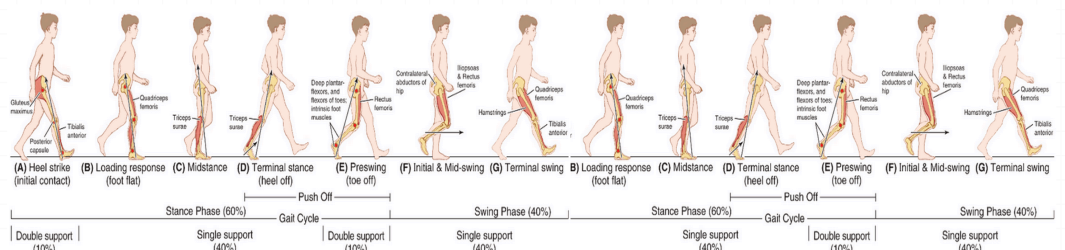
Motivation

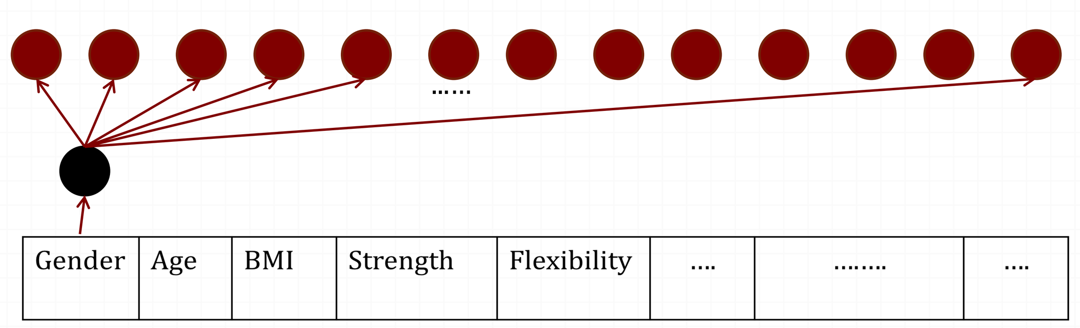


In biomedical applications, time series data frequently co-occur with structured information. Structured covariates, such as patient demographics and measures from clinical examinations, are common and complementary to these time series data. As large amounts of these other sources of data are available, we introduce time series models which integrate and analyze them.

Problem Setup

Interplay between time series and structured information

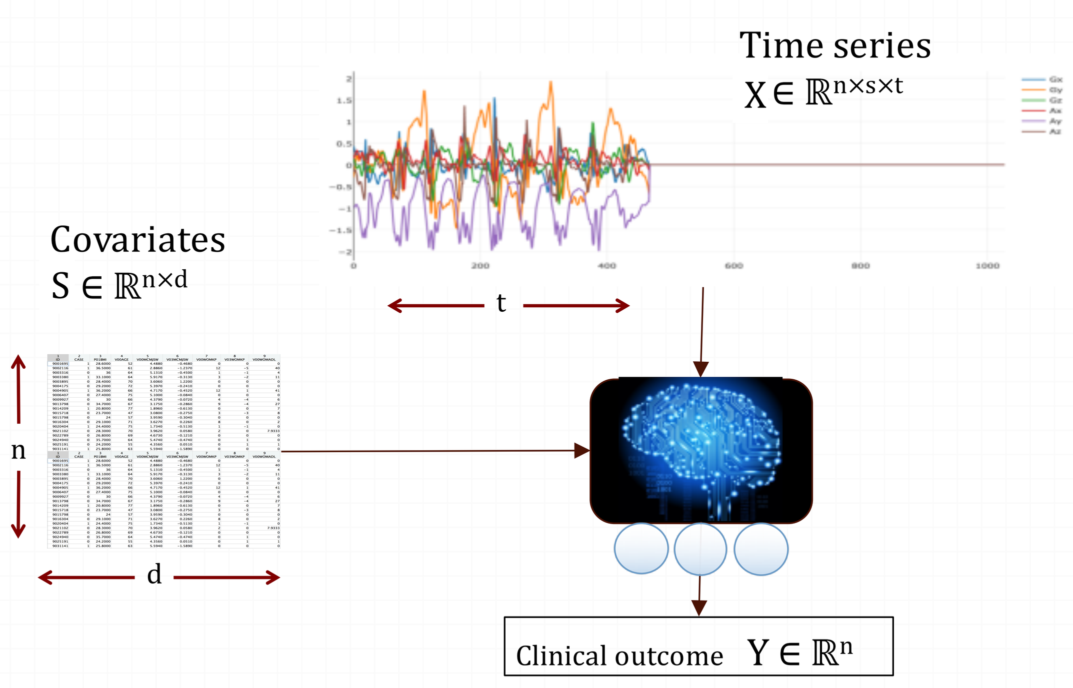




Is toe walking normal?
It depends on the age.

Parameters corresponding to the structured covariates should be shared across the temporal domain.

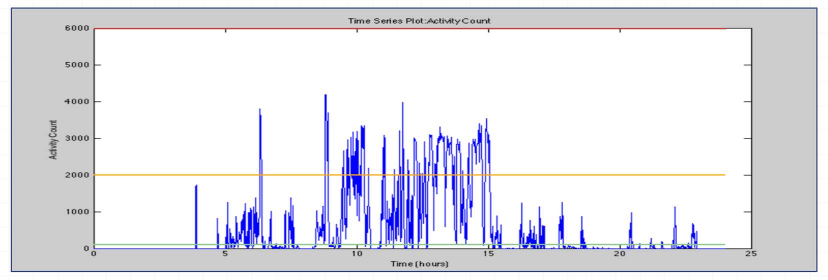
We have a design matrix S with n samples and d covariates as well as a multivariate time series X, which contains s sequences measured over t time points for each sample. For the experiments show here, the output Y is binary and represents the predicted clinical outcome.



Predicting osteoarthritis progression

Osteoarthritis Initiative Dataset (OAI) – 1926 subjects, expressed as activity counts.

Accelerometer data - 7-day activity counts. 650 covariates, out of which we selected 50.



Joint symptoms/function
Medical history
Nutrition
Physical exam, measurements
Subject characteristics, risk factors

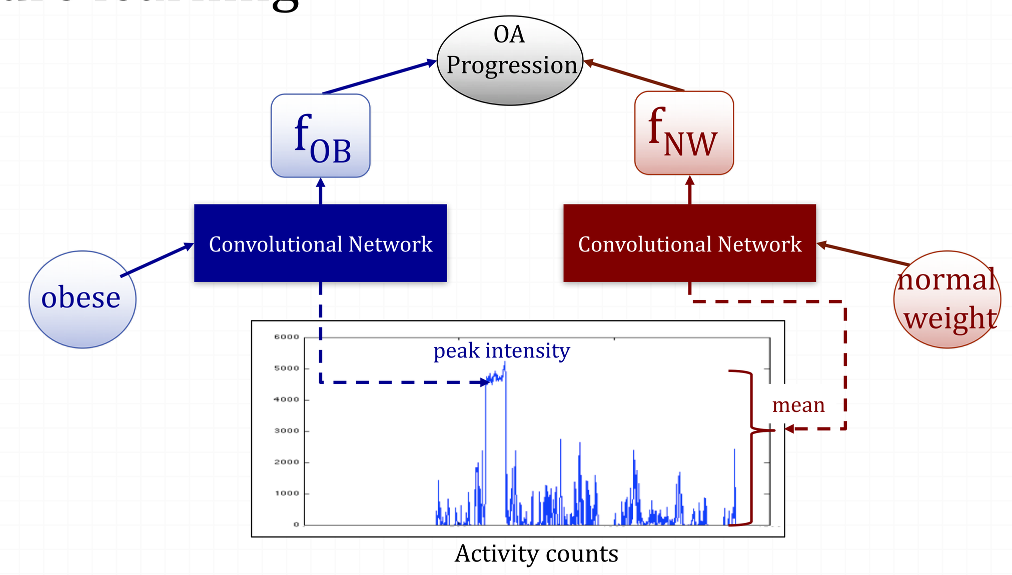
The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health (NIH).

Task: Predict whether subjects are at risk for OA progression.

Output: Joint space narrowing (JSN) > 0.7mm.

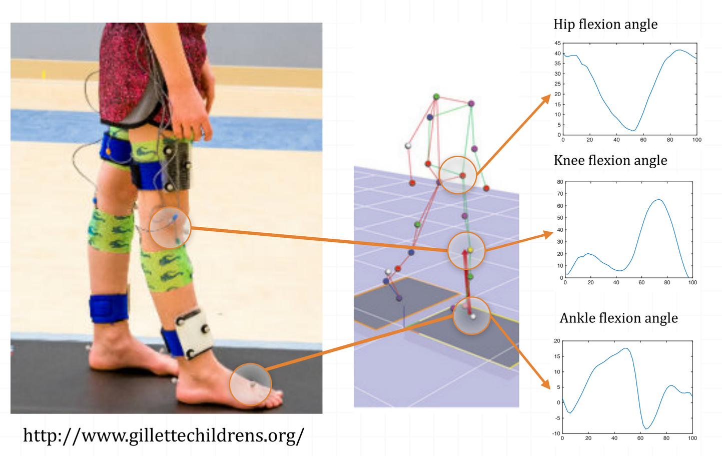
Impact of covariates on feature learning

Example: two subjects with osteoarthritis, but different body mass index (BMI) values. Obese subject has higher weight to height ratio, so intense activity may cause detrimental loading of the joint. For the healthy subject, the mean or minimum activity intensity is more predictive.

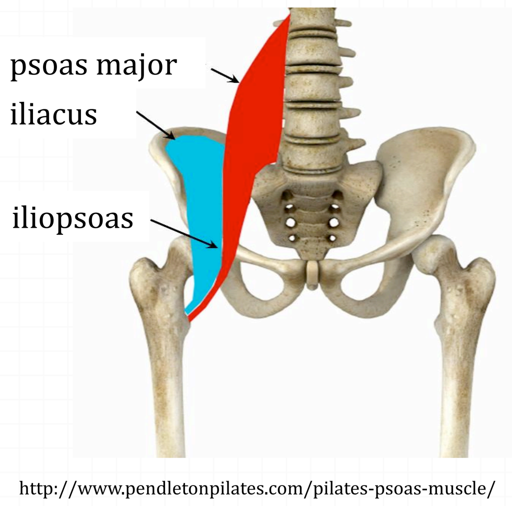


Predicting surgery outcome for patients with cerebral palsy

Gait kinematics: joint angles computed from marker trajectories.



236 subjects. 15 structured covariates.	
Functional Assessment Questionnaire	Discrete
Gross Motor Function Classification System	Discrete
Demographics: Gender	Binary
Demographics: Age	Continuous
Physical: Height, Mass, BMI, Leg length	Continuous
Physical: Pre-surgical PHiDI	Continuous
Spatiotemporal: Cadence, Speed, Step length	Continuous
Spatiotemporal: Side	Binary
Medical history: Quadriplegic, Triplegic	Binary



Surgical treatment (skeletal, muscular) is invasive. Results vary greatly, making treatment planning difficult.

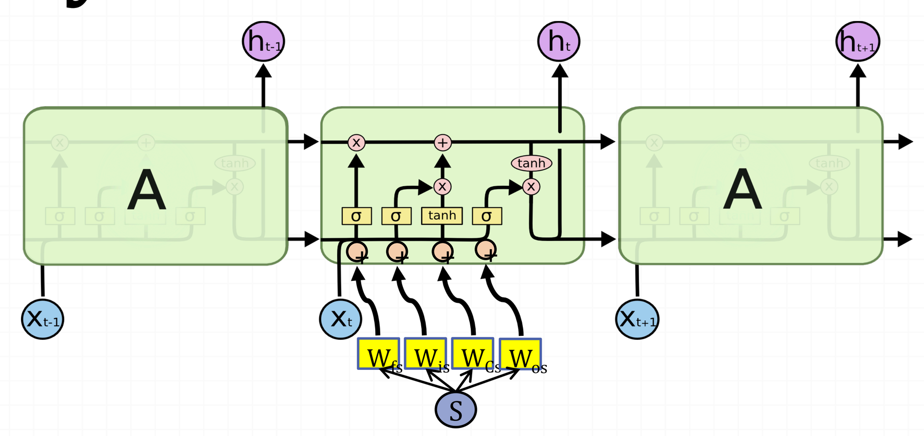
Will psoas lengthening surgery have a positive outcome?

- > 5 improvement in Pelvis and Hip Dev. Index (PHiDI)

OR

- post-surgical Gait Deviation Index (GDI) > 90

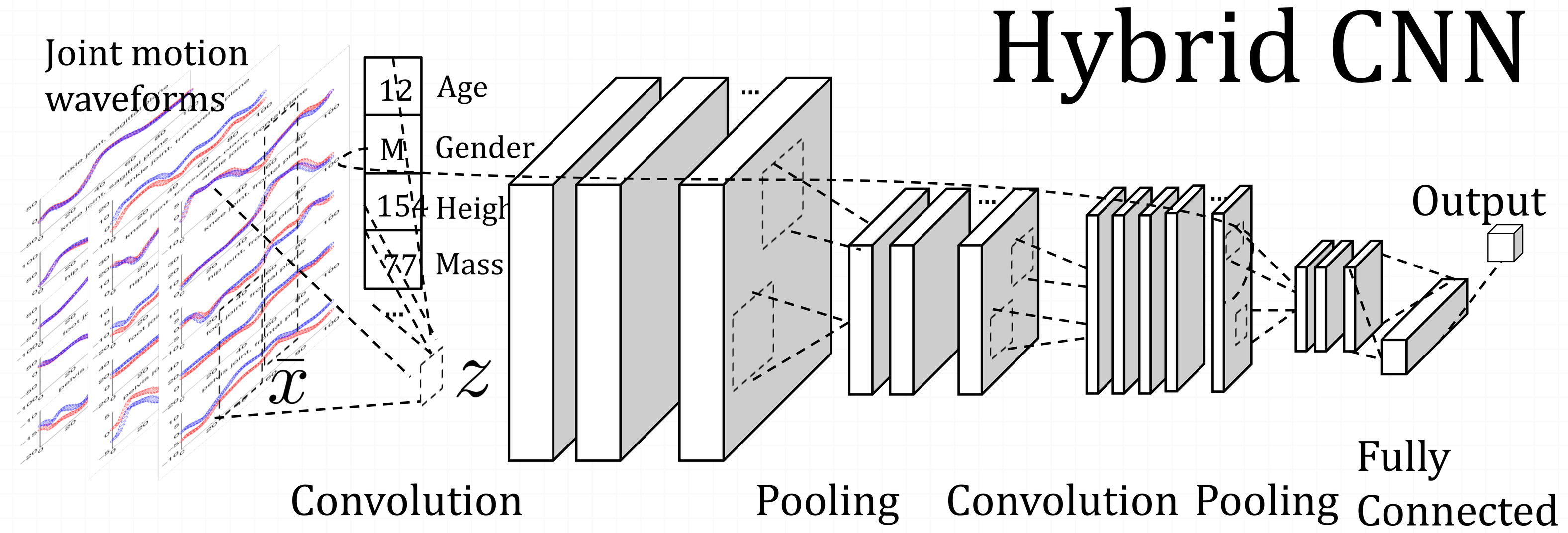
Hybrid LSTM



For LSTM-based architectures, the structured covariates are used internally by the LSTM as part of additive terms in the computation of the nonlinearities.

Weights shared across LSTM cells: W_{fs} (forget gate), W_{is} (input gate), W_{Cs} (state change), W_{os} (output gate).

Hybrid CNN



Covariates are incorporated in the convolutional kernel. Each filter uses a different set.

$\forall i \in [m]$, let V^i be a vector of $\bar{n}$ samples drawn uniformly without replacement from $[n]$.

T^j is the vector of indices of size $\bar{t}$ centered on j.

$$\bar{x}^{ij} = x_{[V^i;T^j]} \qquad \beta = \sum_{i=1}^{d} b_i s_i + b^0$$

$$z_{i,j} = \mathbf{1}^T(\bar{x}^{ij} \circ \kappa)\mathbf{1} + \beta \qquad \kappa_{ij} = w^0_{i,j} + \sum_{\ell}^{[d]} w_{i,j,\ell} s_{r_\ell}$$

Performance

	Cov.	Time series	Osteoarthritis Progression	Psoas Outcome Prediction
Class imbalance	-	-	63.37% ****	65.25% ****
Feature engineering, Covariates, Random Forests	✔	✔	67.10% ****	**78%**
Multiple kernel learning with covariates	✔	✔	68.22% **	76.42% **
Dynamic time warping with covariates	✔	✔	71.54% *	72.33% *
Conditional LSTM	-	✔	72.53% *	74.33% *
Multiresolution CNN	-	✔	71.15% *	74.58% *
Late Fuse	✔	✔	70.30% **	76.17% **
Short Fuse	✔	✔	**74.42%**	**78.92%**

* Statistically significant p<0.05; ** Very significant p<0.01; **** Extremely significant p<0.0001.

CP: **Matched state of the art** without the need for feature engineering.
OA: Accuracy **improved by 7%** compared to models tested in prior work, 3% better than closest contenders.

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