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# Outline Motivation: Big Data Analytics Challenges Complex-Time (kime) Spacekime Calculus & Math Foundations Open Spacekime Problems Neuroscience Applications Longitudinal Neuroimaging (UKBB, fMRI)



# Big Data Characteristics & Challenges

IBM Big Data 4V's: Volume, Variety, Velocity & Veracity				
Big Bio Data Dimensions	Specific Challenges			
Size	Harvesting and management of vast amounts of data			
Complexity	Wranglers for dealing with heterogeneous data			
Incongruency	Tools for data harmonization and aggregation			
Multi-source	Transfer, joint multivariate representation & modeling			
Multi-scale	Interpreting macro $\rightarrow$ meso $\rightarrow$ micro $\rightarrow$ nano scale observation			
Time	Techniques accounting for longitudinal effects (e.g., time co			
Incomplete	Reliable management of missing data, imputation, obfuscation			

 $\hat{f}(\boldsymbol{x},$ 

Example: analyzing observational data of 1,000's Parkinson's disease patients based on 10,000's signature biomarkers derived from multi-source imaging, genetics, clinical, physiologic, phenomics and demographic data elements

Software developments, student training, service platforms and methodological advances associated with the Big Data Discovery Science all present existing opportunities for learners, educators, researchers, practitioners and policy makers

Gao et al., SciRep (2018)



# The Fourier Transform

By separability, the classical **spacetime Fourier transform** is just four Fourier transforms, one for each of the four spacetime dimensions, (x, t) = (x, y, z, t). The FT is a function of the <u>angular</u> <u>frequency</u>  $\omega$  that propagates in the wave number direction **k** (<u>space frequency</u>). Symbolically, the forward and inverse Fourier transforms of a 4D (n = 4) spacetime function f, are defined by:

$$FT(f) = \hat{f}(\mathbf{k},\omega) = \frac{1}{(2\pi)^{\frac{n}{2}}} \int f(\mathbf{x},t)e^{i(\omega t - \mathbf{k}x)} dt d^{3}x,$$
  

$$IFT(\hat{f}) = \hat{f}(\mathbf{x},t) = \frac{1}{(2\pi)^{\frac{n}{2}}} \int \hat{f}(\mathbf{k},\omega)e^{-i(\omega t - \mathbf{k}x)} d\omega d^{3}\mathbf{k}.$$
  

$$) = IFT(\hat{f}) = IFT(FT(f)) = f(\mathbf{x},t), \quad \forall z \in \mathbb{C}, z = \underline{A} e^{i\frac{phase}{q}}$$





Kaluza-Klein Theory

- Theodor Kaluza (1921) developed a math extension of the classical general relativity theory to 5D. This included the metric, the field equations, the equations of motion, the stressenergy tensor, and the cylinder condition. Physicist Oskar Klein (1926) interpreted Kaluza's 3D+2D theory in quantum mechanical space and proposed that the fifth dimension was curled up and microscopic.
- □ The topology of the 5D Kaluza-Klein spacetime is  $K_2 \cong M^4 \times S^1$ , where  $M^4$  is a 4D Minkowski spacetime and  $S^1$  is a circle (non-traversable).









#### The Spacekime Manifold

- □ Spacekime:  $(x, k) = \left(\underbrace{x^1, x^2, x^3}_{\text{Point in space}}, \underbrace{c\kappa_1 = x^4, c\kappa_2 = x^5}_{\text{Moment in kime}}\right) \in X, \ c \sim 3 \times 10^8 \ m/s$ □ Kevents (complex events): points (or states) in the spacekime manifold X. Each kevent is defined by where (x = (x, y, z)) it occurs in space, what is its *causal longitudinal order*
- Spacekime interval (ds) is defined using the general Minkowski 5  $\times$  5 metric tensor  $\left(\lambda_{ij}
  ight)_{i=1,j=1}^{5,5}$  , which characterizes the geometry of the (generally curved) spacekime

$$ds^{2} = \sum_{i=1}^{S} \sum_{j=1}^{S} \lambda_{ij} dx^{i} dx^{j} = \lambda_{ij} dx^{i} dx^{j}$$

$$(\lambda_{ij})$$

- Euclidean (flat) spacekime metric corresponds to the tensor:
  - C0 0 0 0 − 1 Spacelike intervals correspond to ds<sup>2</sup> > 0, where an inertial frame can be found such that two kevents a, b ∈ X are simultaneous. An object can't be present at two kevents which are separated by a spacelike interval.











# Ultrahyperbolic Wave Equation -Cauchy Initial Data Nonlocal constraints yield the existence, uniqueness & stability of local and global solutions to the ultrahyperbolic wave equation under Cauchy initial data ... $\underbrace{ \begin{bmatrix} u_o = u \\ \mathbf{x} \in D_s \end{bmatrix}}_{u_1 = \partial_{\kappa_1} u(\mathbf{x}, \mathbf{0}, \mathbf{\kappa}_{-1})} = f(\mathbf{x}, \mathbf{\kappa}_{-1}) = f(\mathbf{x}, \mathbf{\kappa}_{-1}) = g(\mathbf{x}, \mathbf{\kappa}_{-1})$ $\sum_{\substack{\ell=1\\\text{spatial Laplacian}}}^{d_{\ell}} \partial_{x_{\ell}}^2 u \equiv \Delta_{\mathbf{x}} u(\mathbf{x}, \mathbf{\kappa}) = \underbrace{\Delta_{\mathbf{\kappa}} u(\mathbf{x}, \mathbf{\kappa})}_{\text{tenporal Laplacian}} \equiv \underbrace{\Delta_{\mathbf{\kappa}} u(\mathbf{x}, \mathbf{\kappa})}_{\text{temporal Laplacian}} = \underbrace{\Delta_{\mathbf{\kappa}} u(\mathbf{x}, \mathbf{\kappa})}_{\text{tempora Laplacian}} = \underbrace{\Delta_{\mathbf{\kappa}} u(\mathbf{x}, \mathbf{\kappa})}_{\text{tempora Laplaci}} = \underbrace{\Delta_{\mathbf{\kappa}} u(\mathbf{x}, \mathbf{\kappa})}_{\text{tempora Laplac$ initial conditions (Cauchy Data) Stable local solution over a Fourier frequency region defined by $|\xi| \ge |\eta_{-1}| \dots \underline{nonlocal \ constraints}$ : $\hat{u}\left(\underline{\xi}, \underline{\kappa_{1}, \eta_{-1}}_{\pi}\right) = \cos\left(2\pi \kappa_{1}\sqrt{|\xi|^{2} - |\eta_{-1}|^{2}}\right) \underbrace{\hat{u}_{o}(\xi, \eta_{-1})}_{C_{1}} + \sin\left(2\pi \kappa_{1}\sqrt{|\xi|^{2} - |\eta_{-1}|^{2}}\right) \underbrace{\hat{u}_{1}(\xi, \eta_{-1})}_{2\pi\sqrt{|\xi|^{2} - |\eta_{-1}|^{2}}} \underbrace{\hat{u}_{0}(\xi, \eta_{-1})}_{C_{1}} + \frac{1}{2\pi} \underbrace{\hat{u}_{1}(\xi, \eta_{-1})}_{C_{1}} + \frac{1}$ where $\mathcal{F} \begin{pmatrix} u_o \\ u_1 \end{pmatrix} = \begin{pmatrix} \hat{u}_o \\ \hat{u}_1 \end{pmatrix} = \begin{pmatrix} \hat{u}_o(\xi, \eta_{-1}) \\ \hat{u}_1(\xi, \eta_{-1}) \end{pmatrix} = \begin{pmatrix} \hat{u}(\xi, \eta_{-1}) \\ \partial_{\kappa_1} \hat{u}(\xi, \eta_{-1}) \end{pmatrix}$



#### (Many) Spacekime Open Math Problems Ergodicity

Let's look at particle velocities in the 4D Minkowski spacetime (X), a measure space where gas particles move spatially and evolve longitudinally in time. Let  $\mu = \mu_x$  be a measure on X,  $\underline{f(x,t)} \in L^1(X,\mu)$  be an integrable function (e.g., <u>velocity</u> of a particle), and  $\underline{T}: X \to X$  be a measure-preserving <u>transformation</u> at position  $x \in \mathbb{R}^3$  and time  $t \in \mathbb{R}^+$ 

A pointwise ergodic theorem argues that in a measure theoretic sense, the average of fover all particles in the gas system at a fixed time,  $\bar{f} = E_t(f) = \int_{\mathbb{R}^3} f(\mathbf{x}, t) d\mu_{\mathbf{x}}$ , will be equal to the average velocity (f) of just one particle (x) over the entire time span,

 $\tilde{f} = \lim_{n \to \infty} \left( \frac{1}{n} \sum_{i=0}^{n} f(T^{i} \mathbf{x}) \right)$ , i.e., (show)  $\bar{f} \equiv \tilde{f}$ .

The spatial probability measure is denoted by  $\mu_x$  and the transformation  $T^i x$  represents the dynamics (time evolution) of the particle starting with an initial spatial location  $T^{o}x = x$ .

Investigate the ergodic properties of various transformations in the 5D spacekime  $\vec{f} \equiv E_{\kappa}(f) = \frac{1}{\mu_{\kappa}(X)} \int f\left(x, \underline{t}, \underline{\phi}\right) d\mu_{\kappa} \stackrel{?}{\equiv} \lim_{t \to \infty} \left(\frac{1}{t} \sum_{t=0}^{t} \left(\int_{-\pi}^{+\pi} f(T^{t}x, t, \phi) d\Phi\right)\right) \equiv \vec{f}$ space averaging



#### Mathematical-Physics $\Rightarrow$ Data/Neuro Sciences

#### Mathematical-Physics

A <u>particle</u> is a small localized object that permits observations and characterization of its physical or chemical properties

An **<u>observable</u>** a dynamic variable about particles that can be measured Particles that can be more that a particle Particle state is an observable particle characteristic (e.g., position, momentum) Particle <u>system</u> is a collection of independent particles and observable characteristics, in a closed system Wave-function

Reference-Frame transforms (e.g., Lorentz) State of a system is an observed measurement of all particles ~ wavefunction A particle system is computable if (1) the system is logical, consistent, complete and (2) the unknown internal states of the system don't influence the computation (wavefunction, intervals, probabilities, etc.)

#### **Data/Neuro Sciences**

An <u>object</u> is something that exists by itself, actually or potentially, concretely or abstractly, physically or incorporeal (e.g., person, subject, etc.) A <u>feature</u> is a dynamic variable or an attribute about an object that can be measured

Datum is an observed quantitative or qualitative value, Problem, aka Data System, is a collection of independent objects and features, without necessarily

being associated with apriori hypotheses Inference-function

<u>Data transformations</u> (e.g., wrangling, log-transform) <u>Dataset (data)</u> is an observed instance of a set of datum elements about the problem system,  $O = \{X, Y\}$ 

Computable data object is a very special representation of a dataset which allows direct application of computational processing, modeling analytics, or inference based on the observed data



# Spacekime Analytics

 Kime extension of Time, and
 Parallels between wavefunctions ↔ inference functions Often, we can't directly observe (record) data natively in 5D spacekime. Yet, we can measure quite accurately the kime-magnitudes (r) as event orders, "times". To reconstruct the 2D spatial structure of kime, borrow tricks used by crystallographers to resolve the structure of atomic particles by only observing the magnitudes of the diffraction pattern in k-space. This approach heavily relies on (1) prior information about the kime directional orientation (that may be obtained from using similar datasets and phase-aggregator analytical strategies), or (2) experimental reproducibility by repeated confirmations of the data analytic results using longitudinal datasets. 5D Spacekime 5D k-space 3D Space  $\mathbb{R}^3$ 3D Space  $\mathbb{R}^3$  $(x_1, x_2, x_3)$  $(f_1, f_2, f_3)$ d or Computed Computed **2D** Kime  $\cong \mathbb{R}^2$ K2 Kaluza-Klein $\cong \mathbb{R}^2$  $(x_4, x_5)$ (time(t)), phase( $\phi$ ) Cor



#### *Spacekime* Analytics: Kime-series = Surfaces (not curves)

In the 5D spacekime manifold, time-series curves extend to kime-series, i.e., surfaces parameterized by kimemagnitude (t) and the kimephase ( $\varphi$ ).

Kime-phase aggregating operators that can be used to transform standard time-series curves to spacekime kimesurfaces, which can be modeled, interpreted, and predicted using advanced spacekime analytics.







### **Bayesian Inference Representation**

- □ Suppose we have a single spacetime observation  $X = \{x_{i_0}\} \sim p(x \mid \gamma)$  and  $\gamma \sim p(\gamma \mid \varphi = \text{phase})$  is a process parameter (or vector) that we are trying to estimate.
- □ Spacekime analytics aims to make appropriate inference about the process *X*.
- □ The <u>sampling distribution</u>,  $p(x | \gamma)$ , is the distribution of the observed data *X* conditional on the parameter  $\gamma$  and the <u>prior distribution</u>,  $p(\gamma | \varphi)$ , of the parameter  $\gamma$  before the data *X* is observed,  $\varphi = \text{phase aggregator}$ .
- □ Assume that the hyperparameter (vector)  $\varphi$ , which represents the kime-phase estimates for the process, can be estimated by  $\hat{\varphi} = \varphi'$ .
- Such estimates may be obtained from an oracle (model distribution), approximated using similar datasets, acquired as phases from samples of analogous processes, derived via some phase-aggregation strategy, or computed via Laplace transform.
- □ Let the <u>posterior distribution</u> of the parameter  $\gamma$  given the observed data  $X = \{x_{t_0}\}$  be  $p(\gamma|X, \varphi')$  and the process parameter distribution of the kime-phase hyperparameter vector  $\varphi$  be  $\gamma \sim p(\gamma | \varphi)$ .



# **Bayesian Inference Representation**



- In Bayesian terms, the posterior probability distribution of the unknown parameter y is proportional to the product of the likelihood and the prior.
- □ In probability terms, the posterior = likelihood times prior, divided by the observed evidence, in this case, a single spacetime data point,  $x_{i_0}$ .



#### **Bayesian Inference Representation**

- □ Spacekime analytics based on a single spacetime observation *x*<sub>i₀</sub> can be thought of as a type of Bayesian prior-predictive *or* posterior-predictive distribution estimation problem.
  - $\begin{array}{||c|||} \hline \underline{Prior\ predictive\ distribution\ of\ a\ new\ data\ point\ x_{j_a},\ marginalized\ over\ the\ prior\ -i.e.,\ the\ sampling\ distribution\ p(x_{j_a}|\varphi')\ weight-averaged\ by\ the\ pure\ prior\ distribution): \\ p(x_{j_a}|\varphi') = \int p(x_{j_a}|\gamma) \times \underbrace{p(\gamma|\ \varphi')}_{prior\ distribution\ }d\ \gamma\ . \end{array}$
  - $\label{eq:productive_distribution} \begin{array}{|c|c|c|} \hline \underline{Posterior predictive distribution} \ of a new data point x_{i_o}, marginalized over the$ *posterior* $; i.e., the sampling distribution <math>p(x_{i_o}|\gamma)$  weight-averaged by the *posterior* distribution:  $p(x_{i_o}|x_{i_o}, \varphi') = \int p(x_{i_o}|\gamma) \times \underbrace{p(\gamma|x_{i_o}, \varphi')}_{\text{posterior distribution}} d \gamma \ .$
- □ The difference between these two predictive distributions is that □ the posterior predictive distribution is updated by the observation  $X = \{x_{t_o}\}$  and the
  - hyperparameter, φ (phase aggregator),
     whereas the prior predictive distribution only relies on the values of the hyperparameters that appear in the prior distribution.



## Bayesian Inference Representation

- The posterior predictive distribution may be used to sample or forecast the distribution of a prospective, yet unobserved, data point x<sub>in</sub>.
- The posterior predictive distribution spans the entire parameter statespace (Domain(γ)), just like the wavefunction represents the distribution of particle positions over the complete particle state-space.
- □ Using maximum likelihood or maximum *a posteriori* estimation, we can also estimate an individual parameter point-estimate,  $\gamma_{o}$ . In this frequentist approach, the point estimate may be plugged into the formula for the distribution of a data point,  $p(x | \gamma_{o})$ , which enables drawing IID samples or individual outcome values.



#### **Bayesian Inference Simulation**

- □ Simulation example using 2 random samples drawn from mixture distributions each of  $n_A = n_B = 10$ K observations: □  $\{X_{A,i}\}_{i=1}^{R_A}$ , where  $X_{A,i} = 0.3U_i + 0.7V_i$ ,  $U_i \sim N(0,1)$  and  $V_i \sim N(5,3)$ , and □  $\{X_{B,i}\}_{i=1}^{R_B}$ , where  $X_{B,i} = 0.4P_i + 0.6Q_i$ ,  $P_i \sim N(20,20)$  and  $Q_i \sim N(100,30)$ .
- □ The intensities of cohorts *A* and *B* are independent and follow different mixture distributions. We'll split the first cohort (*A*) into training (*C*) and testing (*D*) subgroups, and then:
  - Transform all four cohorts into Fourier k-space,
  - □ Iteratively randomly sample single observations from (training) cohort *C*,
  - □ Reconstruct the data into spacetime using a single kime-magnitude value and alternative kime-phase estimates derived from cohorts *B*, *C*, and *D*, and
  - □ Compute the classical spacetime-derived population characteristics of cohort A and compare them to their spacekime counterparts obtained using a single C kime-magnitude paired with B, C, or D kime-phases.



### **Bayesian Inference Simulation**

Summary statistics for the original process (cohort A) and the corresponding values of their counterparts computed using the spacekime reconstructed signals based on kime-phases of cohorts B, C, and D. The estimates for the latter three cohorts correspond to reconstructions using a single spacetime observation (i.e., single kime-magnitude) and alternative kime-phases (in this case, kime-phases defronts B, C, and D).

		Spacetime	Spacekime Reconstructions (single kime-magnitude)		
1	Summariae	(A)	(B)	(C)	(D)
	Summaries	Original	Phase=Diff. Process	Phase=True	Phase=Independent
	Min	-2.38798	-3.798440	-2.98116	-2.69808
	1 <sup>st</sup> Quartile	-0.89359	-0.636799	-0.76765	-0.76453
	Median	0.03311	0.009279	-0.05982	-0.08329
	Mean	0.00000	0.000000	0.00000	0.00000
	3 <sup>rd</sup> Quartile	0.75772	0.645119	0.72795	0.69889
	Max	3.61346	3.986702	3.64800	3.22987
1	Skewness	0.348269	0.001021943	0.2372526	0.31398
0.10	Kurtosis	-0.68176	0.2149918	-0.4452207	-0.3270084
dematty	cohort				
0.00- -do d sis vice v value	da 200				

# **Bayesian Inference Simulation**

The correlation between the original data (*A*) and its <u>reconstruction using a single</u> <u>kime magnitude</u> and the correct kime-phases (*C*) is  $\rho(A, C) = 0.89$ .

This strong correlation suggests that a substantial part of the A process <u>energy</u> <u>can be recovered using only a single observation</u>. In this case, to reconstruct the signal back into spacetime and compute the corresponding correlation, we used a single kime-magnitude (sample-size=1) and process *C* kime-phases.



# **Bayesian Inference Simulation**

Let's demonstrate the Bayesian inference corresponding to this spacekime data analytic problem using a simulated bimodal experiment:  $X_A = 0.3U + 0.7V$ , where  $U \sim N(0,1)$  and  $V \sim N(5,3)$ 

Specifically, we will illustrate the Bayesian inference using repeated single spacetime observations from cohort A,  $X = \{x_{i_0}\}$ , and varying kime-phase priors ( $\theta = \text{phase aggregator}$ ) obtained from cohorts B, C, or D, using different posterior predictive distributions.

Relations between the empirical data distribution (dark blue) and samples from the posterior predictive distribution, representing Bayesian simulated spacekime reconstructions (light-blue). The derived Bayesian estimates do not perfectly match the empirical distribution of the simulated data, yet there is clearly information encoding that is captured by the spacekime data reconstructions.

This signal compression can be exploited by subsequent model-based or modelfree data analytic strategies for retrospective prediction, prospective forecasting, ML classification, AI derived clustering, and other spacekime inference methods.

# **Bayesian Inference Simulation** Bayesian simulated spacekime reconstructions Samples from the posterior predictive distribution Distributio ( - X)R Π(r<sub>m</sub>) 100 A IOP (dark blue) and sa rical data distrib light-blue

# Tensor-based Linear Modeling of fMRI

3-tier Analysis: registering the fMRI data into a brain atlas space, 56 ROIs, tensor 3-tier Analysis: registering the fMRI data into a brain atlas space, 56 ROIs, tensor linear modeling, post-hoc FDR processing & selection of large clusters of significant voxels are identified within the important ROIs: Y = (X, B) + E. The dimensions of the tensor Y are  $160 \times a \times b \times c$ , where the tensor elements represent the response variable Y[t, x, y, z], i.e., fMRI intensity. For fMRI magnitude (real-valued signal), the design tensor Y dimensions are:  $160 \times \frac{4}{R} \times \frac{1}{R}$ .



#### Spacekime Analytics: Demos

#### Tutorials

- https://TCIU.predictive.space
- □ <u>https://SpaceKime.org</u>

#### R Package https://cran.rstudio.com/web/packages/TCIU

#### GitHub https://github.com/SOCR/TCIU



