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Latent Bone Modeling Approach to Estimate Plutonium Activity Concentration in Human Skeleton

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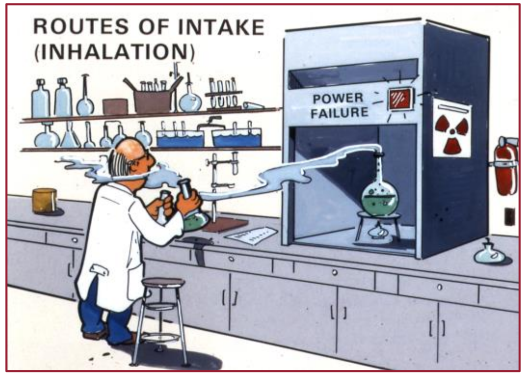
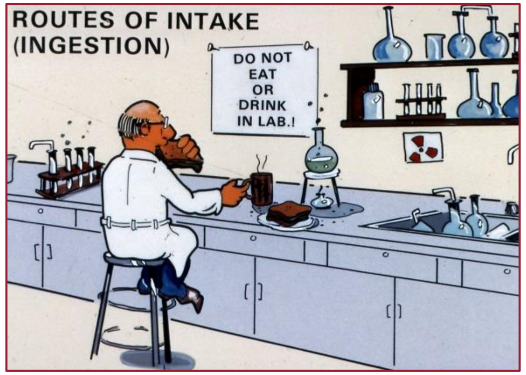
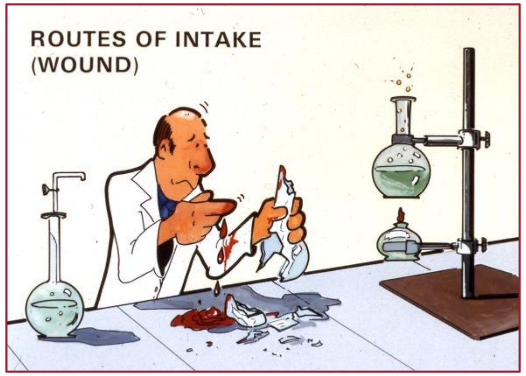
Background

- Plutonium is a bone seeker
- Most of USTUR Registrants had plutonium intakes
- For 19 whole-body cases, right side of the skeleton (up to 90 bones) was analyzed for plutonium
- For 232 partial-body cases, only a selected number of bones (2 to 8) were analyzed for plutonium

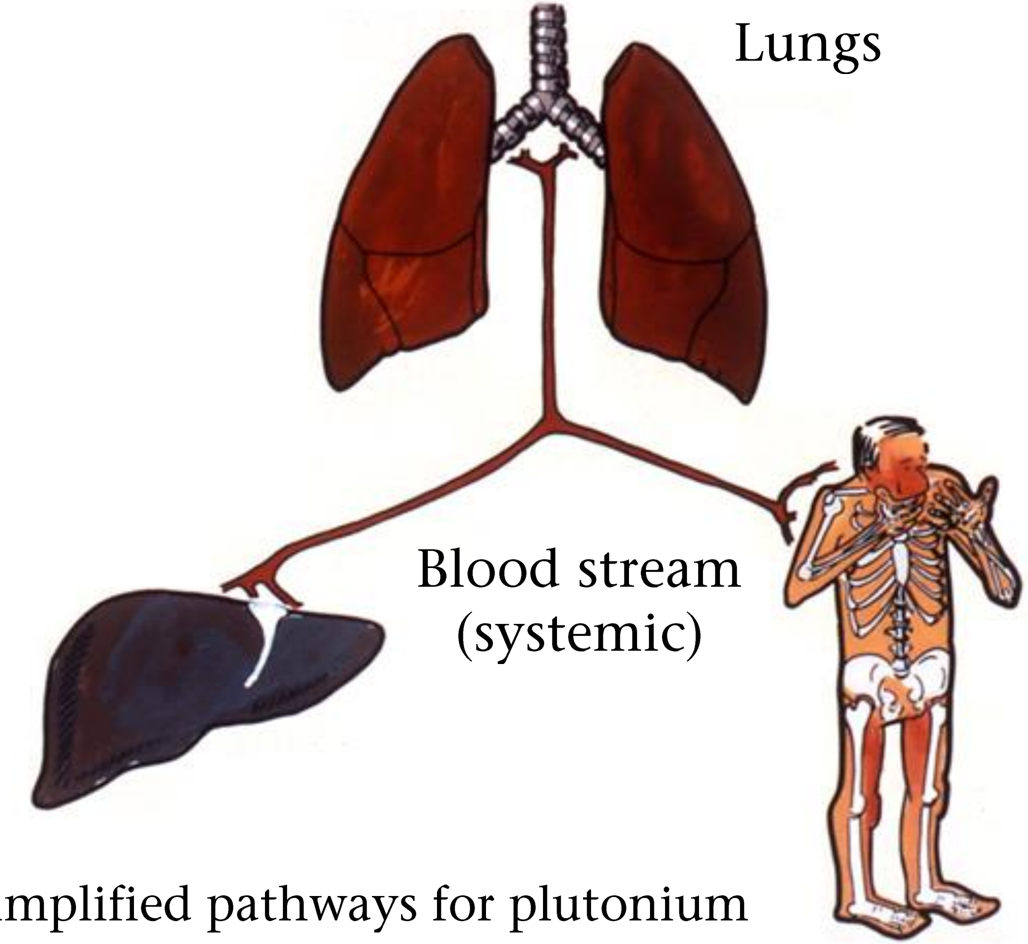
Why Plutonium in the Skeleton?







- Plutonium is a *bone-seeker*



Simplified pathways for plutonium

USTUR Whole-Body Bone Dataset

19 cases × 90 bones

- Cranial: 11
- Trabecular: 18
- Cortical: 29
- Diaphysis†: 14
- Epiphysis‡: 15
- ‘Mixed’§: 3

† - shafts of the long bones; ‡ - ends of the long bones + patella
§ - cervical vertebra #1 whole, hand and wrist, foot and ankle

USTUR Partial-Body Bone Dataset

Total of 232 partial-body cases with 2 – 8 analyzed bone samples

		Analyzed bone group									
		I	II	III	IV	V	VI	VII	VIII	IX	X
Collected bone	**Number**	157	155	123	72	48	40	12	8	7	6
Rib	209	■	■	■	■	■	■	■	■	■	■
Sternum	165	■		■	■	■	■	■	■	■	■
Vertebral body	160		■	■	■	■	■	■	■	■	■
Patella	133				■		■	■	■	■	■
Clavicle	81					■	■	■	■	■	■
Femur shaft	71							■	■	■	■
Calvarium	49								■		■
Femur end	27									■	■

Long Time Practical Research Question

How to estimate skeletal plutonium concentration (C_{skel}) from a selected number of bones?

Estimation of Plutonium in Human Skeleton from Selected Number of Bones

- Published USTUR's studies
  - Lynch TP, Kathren RL, McInroy JF. Macrodistribution of plutonium and americium in four human skeletons. Journal of Radiological Protection 8 (2): 67–76 (1988)
  - Hall CA. Estimation of skeletal deposition of plutonium and americium from a selected bone subset. MS Thesis, Washington State University (1997)
  - Filipy RE, Alldredge JR, Hall CA, McInroy JF, Glover SE, Qualls S. Estimation of actinide skeletal content in humans based on bone samples collected at autopsy. Health Physics 84 (1): 34–45 (2003)
  - Matthews T. Estimation of skeletal plutonium and americium content from bone samples taken at autopsy. MS Thesis, Idaho State University (2009)
  - Tolmachev SY, Avtandilashvili M, Kathren RL. Estimation of total skeletal content of plutonium and ^{241}Am from analysis of a single bone. Health Physics 117 (2): 202–210 (2019)

Linear Regression Approach

- *Assumption*: Linear relationship between plutonium concentration of a bone (C_{bone}) and the total skeleton plutonium concentration (C_{skel})

1. Single bone linear model ('best bone'): $C_{skel} = r \times C_{bone}$
2. Group bone linear model: $C_{skel} = r \times (\sum_{i=1}^{n} C_{bone,\, i})/n$
3. Multiple linear model: $C_{skel} = a_1 \times C_{bone,\, 1} + a_2 \times C_{bone,\, 2} + \ldots + a_n \times C_{bone,\, n}$

Limitations of Multiple Linear Regression (MLR) Approach

- A USTUR study using MLR approach
  - Filipy RE, Alldredge JR, Hall CA, McInroy JF, Glover SE, Qualls S. Estimation of actinide skeletal content in humans based on bone samples collected at autopsy. Health Physics 84 (1): 34–45 (2003)

  Eight (8) whole-body cases were analyzed at the time

- General limitations:
  - Multicollinearity (highly correlated independent variables)
  - Sample size (case-to-variable ratio, 5:1 minimum)
- Imprecise and unstable estimates of the model parameters

Multicollinearity: Correlation Matrix

- Bone samples commonly collected at autopsy: vertebra, rib, sternum, patella, femur middle shaft (MS), and clavicle

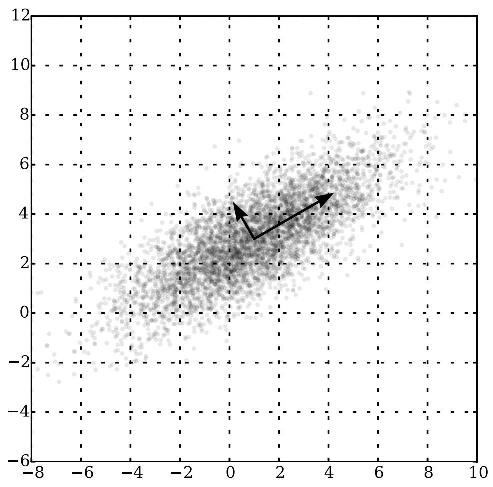
Bone†	Vertebra	Rib	Sternum	Patella	Femur MS	Clavicle
Vertebra	1.00					
Rib	0.98	1.00				
Sternum	0.98	0.96	1.00			
Patella	0.95	0.94	0.94	1.00		
Femur MS	0.93	0.90	0.96	0.97	1.00	
Clavicle	0.97	0.96	0.99	0.96	0.98	1.00

† data from 19 whole-body tissue donations

Principal Component Analysis (PCA)

A statistical technique to reduce the dimensionality of a dataset by finding principal components that are:

1. Preserving maximum possible ‘variability/information’ in original data
2. Linear functions of independent/original variables
3. Orthogonal to each other



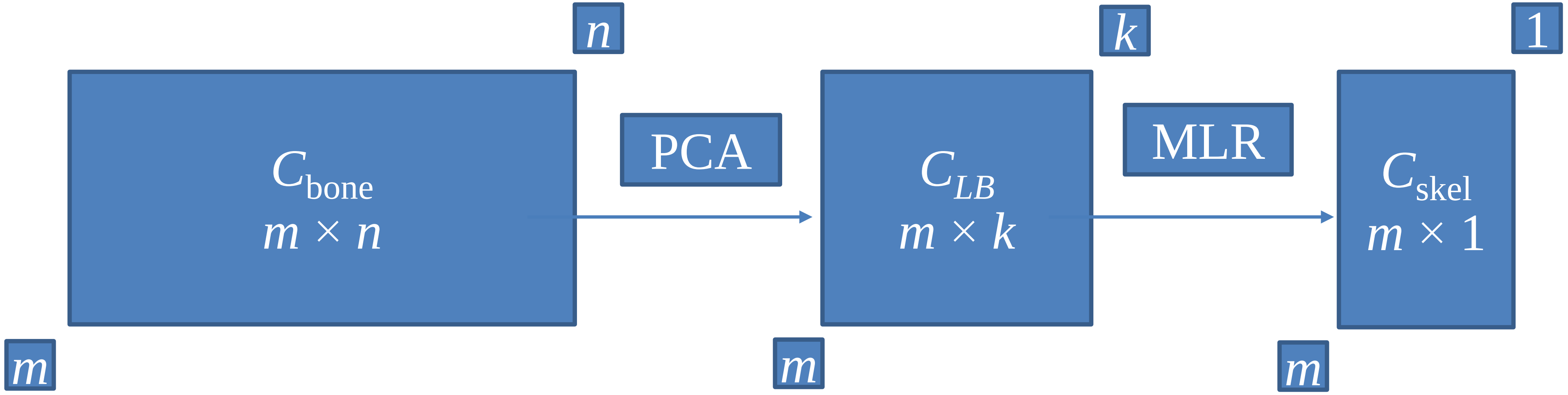
https://commons.wikimedia.org/wiki/File:GaussianScatterPCA.svg

Principal Component Regression (PCR)

- A multiple linear regression (MLR) analysis technique that is based on principal component analysis (PCA)
- In PCR, instead of regressing the dependent variable on the the independent variables directly, principal components are used as regressors
- Typically only the first few principal components are used for regression

In our context, a principal component is called a latent bone (LB), and PCR is called Latent Bone Modeling (LBM)

Principal Component Regression (PCR)
- *Latent Bone Modeling (LBM)* -



m: number of cases
n: number of bones
k: number of latent bone variables

PCA: Principal Component Analysis
MLR: Multiple Linear Regression

Latent Bone Modeling: Example (I)
- USTUR Three Common Collected Bones -

- Three most frequently collected bones: rib, sternum, and vertebra

Bone†	^{239}Pu concentration, Bq kg^{-1} wet																		
Rib	6.1	14.2	23.2	60.4	16.6	3.0	4.8	7.6	15.3	14.0	2.1	30.3	35.4	1.4	106.4	44.5	13.7	82.2	6.4
Sternum	4.7	5.7	17.1	44.8	16.1	2.9	3.2	7.9	7.9	10.5	1.1	22.6	32.7	1.7	117.7	45.8	3.4	52.4	5.4
Vertebra	6.0	19.0	21.5	58.8	19.5	3.9	4.9	9.6	10.2	14.7	1.8	35.8	40.4	1.7	118.2	58.6	11.9	71.7	9.2
Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19

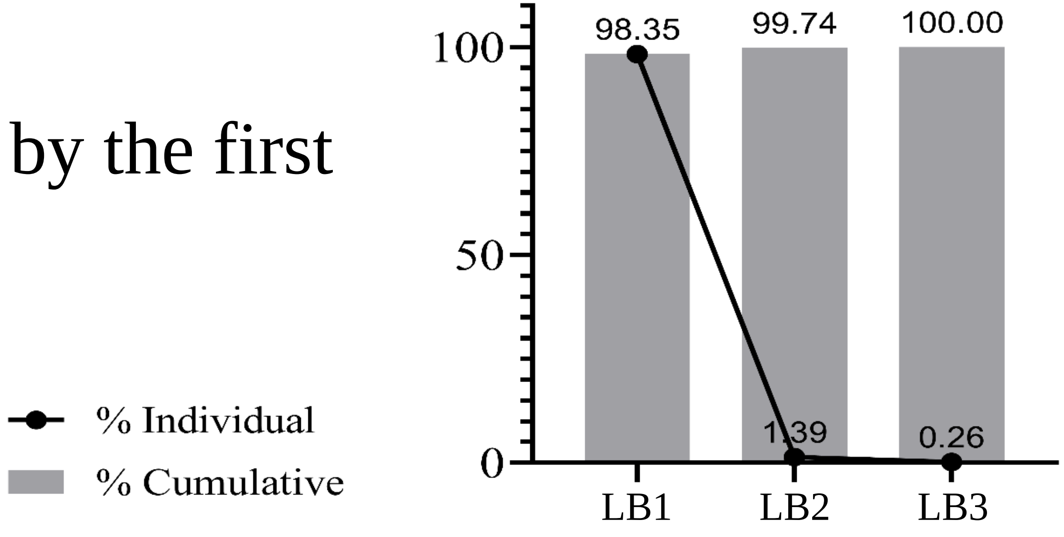
† data from 19 whole-body tissue donation cases

Latent Bone Modeling: Example (II)
- *Principal Component Analysis* -

$$C_{LB1} = 0.5759 \times C^{s}_{\text{rib}} + 0.5755 \times C^{s}_{\text{sternum}} + 0.5807 \times C^{s}_{\text{vert}}$$

- C_{LB1}: the first *latent bone* concentration (19 × 1 vector)
- C^{s}_{rib}, C^{s}_{sternum}, C^{s}_{vert}: standardized individual bone concentrations (19 × 1 vectors)
- $C^{s}_{\text{bone, i}} = (C_{\text{bone, i}} - C_{\text{bone, ave}}) / SD_{\text{bone}}$

- 98.35% of total variance is explained by the first latent bone



Latent Bone Modeling: Example (III)
- *Linear Regression* -

- Principal Component Analysis followed by simple linear regression

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
C_{LB1}	-1.13	-0.7	-0.24	1.77	-0.43	-1.27	-1.2	-0.96	-0.8	-0.69	-1.36	0.28	0.67	-1.36	5.28	1.47	-0.89	2.6	-1.05
C_{skel}	6.0	11.1	20.2	42.0	10.8	2.8	2.8	8.6	14.5	11.0	2.0	29.2	28.0	0.9	122.0	65.3	12.2	76.8	9.0

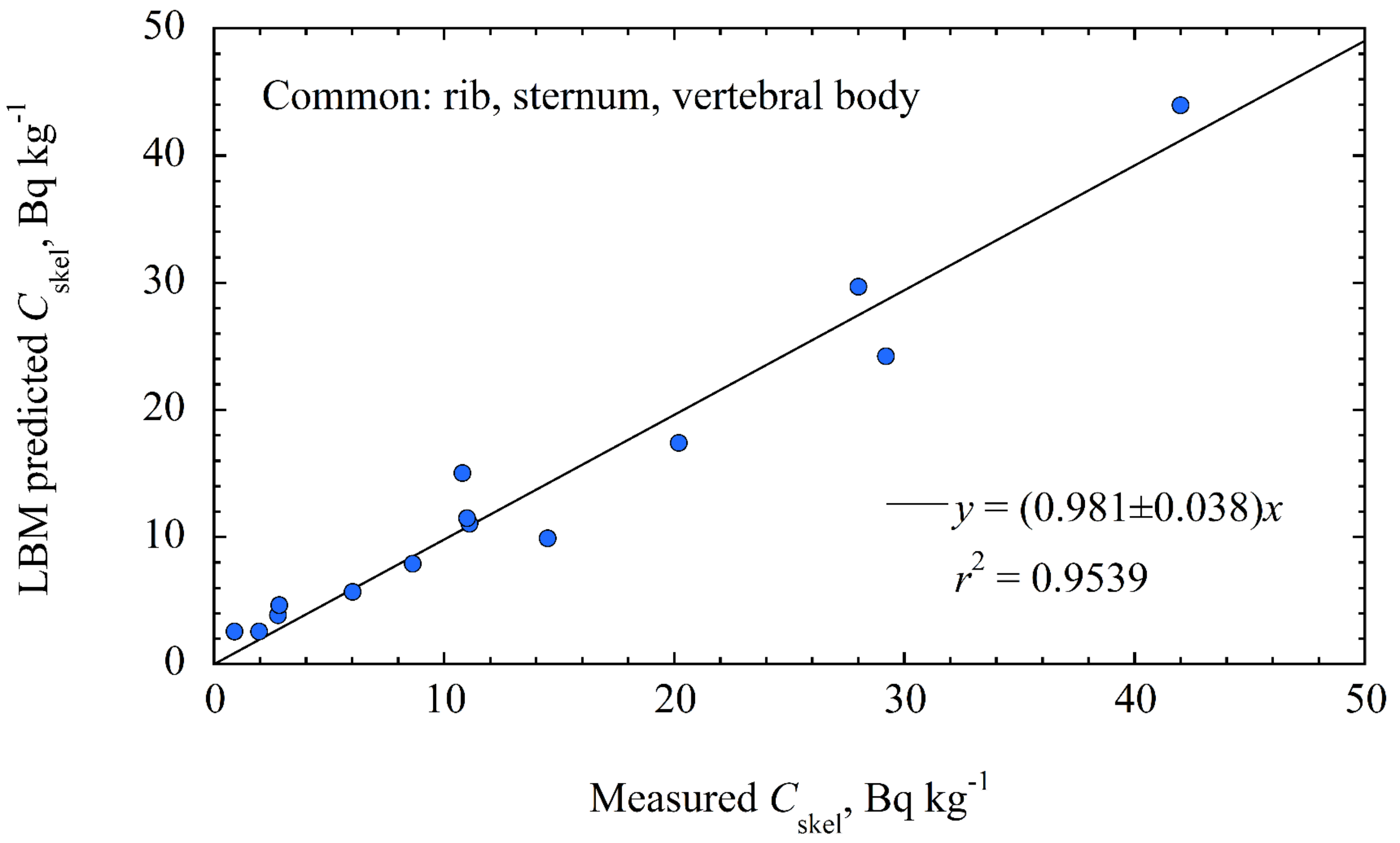
Latent Bone Modeling: Example (IV)
- *Linear Regression* -

- Estimated total skeleton concentration, $C_{\text{skel}} = 18.0 \times C_{\text{LB1}} + 25.0$
- Model statistics
  - Residual standard error (RSE) = 5.995 ($N_{\text{DF}} = 17$)
  - Adjusted $R^2 = 0.9639$

$$RSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{(n - p - 1)}}$$

Latent Bone Modeling: Example (V)

- *Model Evaluation* -



Summary

- LBM approach is introduced and is a preferred method for estimating Pu concentration in the entire skeleton from a selected number of bones
- LBM for one possible bone combination (rib, sternum, and vertebra), most frequently collected bones, was described as an example