Conditional Recurrent Flow: Conditional Generation of Longitudinal Samples with Applications to Neuroimaging
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**Objective:**

Conditional Invertible Neural Network (Ardizzoni et al., 2019): a conditional invertible mapping between \( x \to y \) using Coupling Layer (Actnorm + Invertible Neural Network).

**Preliminary 1:** Normalize Flow and Coupling Layer

Normalizing Flow: Maps a sample \( x \) to a target variable \( z \sim f(x) \) where \( z \) is from a standard normal distribution \( Z \). \( q(\cdot) \sim n(\mu, \sigma) \), \( | \partial f/\partial x | \in \mathbb{R}^+ \) where \( \Delta \) is a Jacobian determinant.

Coupling Layer [Dinh et al., 2016]: Allows an exactly invertible mapping \( u \to v \) with subnetworks \( r \) and \( s \).

1. Forward map (Fig. (a)):
   
   \[ u \rightarrow v \mid \begin{align*}
   v_{1} &= u_{1} \\
   v_{2} &= u_{2} + \log \left( \frac{u_{2}}{u_{1}} \right)
   \end{align*} \]

2. Inverse map (Fig. (b)):
   
   \[ u \rightarrow v \mid \begin{align*}
   u_{1} &= \exp(v_{1}) \\
   u_{2} &= \exp(v_{2}) - \exp(v_{1})
   \end{align*} \]

**Method 1:**

Given: Sequential data \( x^{1}, x^{2}, \ldots, x^{T} \) and label/covariate \( y \).

1. Forward Map:
   
   \[ x^{t} \rightarrow (u_{1}^{t}, u_{2}^{t}) \rightarrow (u_{1}^{t}, u_{2}^{t}) \rightarrow (v_{1}^{t}, v_{2}^{t}) \rightarrow y^{t} \]

2. Inverse Map:
   
   \[ (u_{1}^{t}, u_{2}^{t}) \rightarrow (v_{1}^{t}, v_{2}^{t}) \rightarrow (u_{1}^{t}, u_{2}^{t}) \rightarrow x^{t+1} \]

**Method 2:**

Conditional Recurrent Flow (CrOW) [Hwang et al., 2019]:

1. Forward Map:
   
   \[ (u_{1}^{t}, u_{2}^{t}) \rightarrow (v_{1}^{t}, v_{2}^{t}) \rightarrow (u_{1}^{t}, u_{2}^{t}) \rightarrow y^{t} \]

2. Inverse Map:
   
   \[ (u_{1}^{t}, u_{2}^{t}) \rightarrow (v_{1}^{t}, v_{2}^{t}) \rightarrow (u_{1}^{t}, u_{2}^{t}) \rightarrow x^{t+1} \]

**Experiment 2:**

1. **Neuroimaging for Alzheimer’s Disease**
   
   Q: Can we detect the differences in the Alzheimer’s disease (AD) pathology progression between groups with “Normal” and “Abnormal” covariates? (idea illustrated in Fig. of Motivation Sec.)

   - Dataset: \( N \sim 276 \) Amyloid PET images (AV45) of T = 3 time points from Alzheimer’s Disease Neuroimaging Initiative (ADNI) in 62 DooKan Alius regions
   - 1. Longitudinal region-wise amyloid measures: \( x^{t} \sim 2^{0.2} \) for \( t = 1 \) to 2.3
   - 2. Longitudinal covariates: \( y \in \mathbb{R}^{T} \)

   **Analysis Setup:** For each covariate type,
   
   - (1) Training: Train with all \( N \sim 276 \) subjects
   - (2) Generation: Generate (i) Group A: 100 samples of \( x \) given “Normal” \( y \) and (ii) Group B: 100 samples of \( x \) given “Abnormal” \( y \)
   - Statistical Analysis: At 1 – 3, perform a group difference test between Group A and Group B in each region. Count significantly differences regions.

   - **Measure of Generation:** Average of Distance Scores
   - **Measure of Real Data Scores:** Average of Real Data Scores

   - **Summary:** How well did CrOW improve the statistical analysis? Can we detect \( \Delta \) for which type of patients?