Estimating Timescale Maps with Functional MRI

Motivations

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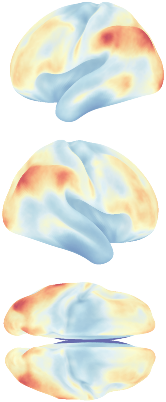
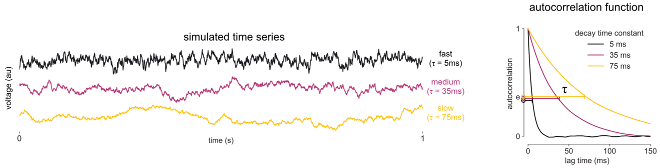
Supplementary



Scientific Motivation

Neural timeseries often exhibit time-lagged correlation that is characterized by autocorrelations that decay exponentially.

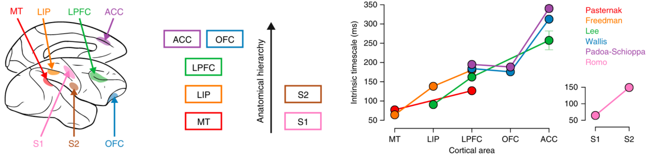
The timescale parameters (τ) controls the decay rate.



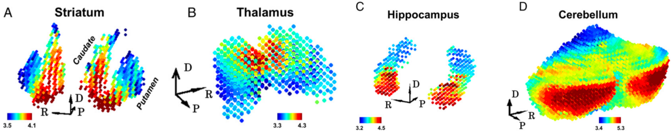
(Gao et al. 2020)

Timescale Organization

Timescales follow a hierarchy from sensory to associative regions of cortex (Murray et al. 2014).



This pattern repeats itself in subcortical regions (Raut et al. 2020; Müller et al. 2020; Nougaret et al. 2021).



Timescale Functional Roles

Experimental Conditions

- Pharmacological agents: Propofol (Huang et al. 2018) and Serotonergic drugs (Shinn et al. 2023).
- Working memory tasks (Gao et al. 2020).
- Sleep deprivation (Meisel et al. 2017).

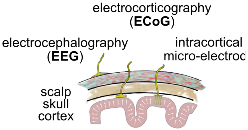
Observational Studies

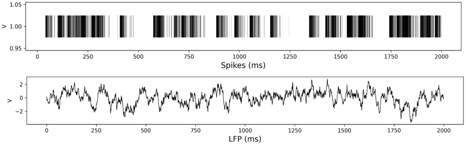
- Ageing (Gao et al. 2020).
- Psychiatric disorders: Autism (Watanabe et al. 2019) and Schizophrenia (Wengler et al. 2020).

Recording Brain Activity

Electrical Signals: EEG, ECoG, iEEG

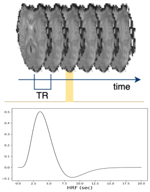
- Dense sampling in time, sparse sampling in space.

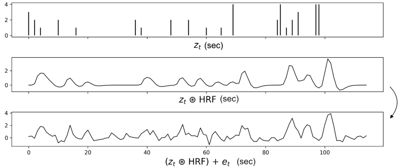




Hemodynamic Signals: fMRI

- Sparse sampling in time, dense sampling in space.

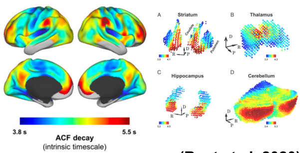




- head motion
- respiratory effects
- cardiac effects
- scanner noise

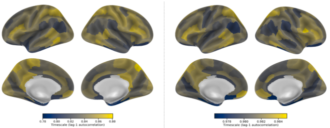
fMRI Timescale Maps

Genomics Superstruct Project



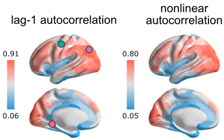
(Raut et al, 2020)

Nathan Kline Institute **Human Connectome Project**



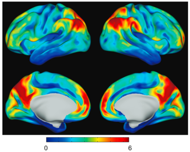
(Lurie et al, 2024)

Human Connectome Project



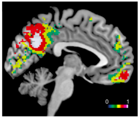
(Shafiei, 2020)

Genomics Superstruct Project



(Mitra et al, 2014)

Human 3T fMRI

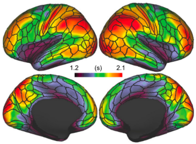


(Kaneoke et al, 2012)

Raut et al. 2020; Lurie et al. 2024; Shafiei et al. 2020; Mitra et al. 2014; Kaneoke et al. 2012

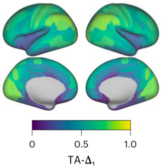
fMRI Timescale Maps

Human Connectome Project



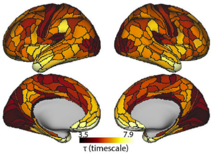
(Wengler et al, 2020)

Human Connectome Project



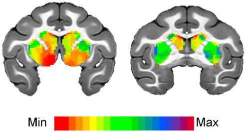
(Shinn et al, 2023)

Human Connectome Project



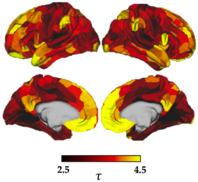
(Ito et al, 2020)

Macaque 10.5T fMRI



(Manea et al, 2022)

Human 7T fMRI



(Muller et al, 2020)

Wengler et al. 2020; Shinn et al. 2023; Ito et al. 2020; Manea et al. 2022; Müller et al. 2020

Timescale Methods

1. **Time Domain** (6/25 papers):
   Kaneoke et al. 2012; Meisel et al. 2017; Huang et al. 2018; Lurie et al. 2024; Shinn et al. 2023; Shafiei et al. 2020

2. **Autocorrelation Domain** (18/25 papers):
   Murray et al. 2014; Rossi-Pool et al. 2021; Cirillo et al. 2018; Ito et al. 2020; Runyan et al. 2017; Zeraati et al. 2022; Nougaret et al. 2021; Wasmuht et al. 2018; Müller et al. 2020; Maisson et al. 2021; Li et al. 2022; Shafiei et al. 2020; Wengler et al. 2020; Manea et al. 2022; Watanabe et al. 2019; Zilio et al. 2021; Raut et al. 2020; Golesorkhi et al. 2021

3. Frequency Domain (3/25 papers):
   Gao et al. 2020; Zeraati et al. 2022; Fallon et al. 2020

Project Objective

Problem Statement:

- Current timescale methods rely on restrictive assumptions about the underlying stochastic process
- Existing research reports point estimates without standard errors, hindering accurate inference and comparisons across brain regions

Proposed Solution:

- Build on existing methods, designed to be robust under general assumptions
- Analyze the statistical properties (bias, consistency, limiting variance) of these estimators

Assumptions

Let $\{X_t, t \in \mathbb{Z}\}$ be a discrete stochastic process that is **weakly stationary** and **ergodic**, and $x_t = \{x_1, x_2, ..., x_T\}$ be a finite sample. Assume X_t and x_t are mean zero.

Stationarity implies:

$$\gamma_k = \text{cov}[X_t, X_{t-k}] = \mathbb{E}[X_t X_{t-k}] \tag{1}$$

Ergodicity implies:

$$\lim_{T\to\infty} \frac{1}{T} \sum_{k=1}^{\infty} \gamma_k = 0 \tag{2}$$

(Hansen 2022)

Autoregressive Model

Example of time domain method.

Def. Autoregressive Model

$$X_t = \phi X_{t-1} + e_t \tag{3}$$

Def. Timescale

$$\phi = (\mathbb{E}[X_{t-1}^2])^{-1}(\mathbb{E}[X_t X_{t-1}]) \tag{4}$$

$$\tau = g(\phi) = -\frac{1}{\log(|\phi|)}. \tag{5}$$

Implies a theoretical ACF that decays exponentially with a rate determined by ϕ: $\rho_k = \phi^k$.

τ determines where the autocorrelations reach $1/e \approx 0.37$.

Autoregressive Model

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τ determines where the autocorrelations reach $1/e \approx 0.37$.

Autoregressive Model

Def. Standard Error of Timescale:

$$\text{se}_{\text{NW}}(\phi) = \sqrt{q^{-1}\omega q{-1}} \tag{6}$$

$$\text{se}_{\text{NW}}(\tau) \approx \text{se}_{\text{NW}}(\phi)\frac{d}{d\phi}g(\phi) \tag{7}$$

where:

$$q = \mathbb{E}[X_{t-1}^2]$$

$$\omega = \sum_{\ell=-\infty}^{\infty} \mathbb{E}[(X_{t-1}e_t)(X_{t-1-\ell}e_{t-\ell})]$$

Newey et al. 1987

Exponential Decay Model

Example of autocorrelation domain method.

Def. Autocorrelation Function:

$$\rho_k = \mathrm{corr}(X_t, X_{t-k}) = \frac{\gamma_k}{\gamma_0} \tag{8}$$

Def. Exponential Decay Model:

$$\rho_k = \phi^k + e_k \tag{9}$$

Def. Timescale:

$$S(\phi) = \mathbb{E}[(\rho_k - \phi^k)^2] \tag{10}$$

$$\phi^* = \underset{\phi}{\mathrm{argmin}}\ S(\phi) \tag{11}$$

$$\tau^* = g(\phi^*) = -\frac{1}{\log(|\phi^*|)} \tag{12}$$

τ^* determines where the autocorrelations reach $1/e \approx 0.37$ (Murray et al. 2014)

Exponential Decay Model

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Exponential Decay Model

Def. Standard Error of Timescale:

$$\text{se}_{\text{NW}}(\phi^*) = \sqrt{q^{-1}\omega q^{-1}} \tag{13}$$

$$\text{se}_{\text{NW}}(\tau^*) \approx \text{se}_{\text{NW}}(\phi^*)\frac{d}{d\phi}g(\phi^*) \tag{14}$$

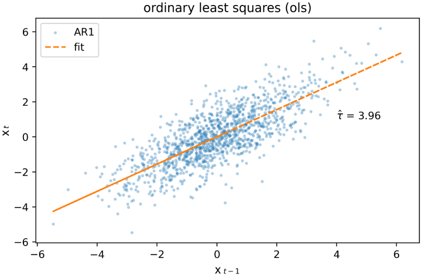
where:

$$\begin{aligned}
m(k,\phi) &= \phi^k \\
m_{\phi,k} &= \frac{d}{d\phi}m(k,\phi) = k\phi^{k-1} \\
q &= \mathbb{E}[m^2_{\phi^*,k}] = \mathbb{E}[(k{\phi^*}^{k-1})^2] \\
\omega &= \sum_{\ell=-\infty}^{\infty} \mathbb{E}[(m_{\phi^*,k}e_k)(m_{\phi^*,k-\ell}e_{k-\ell})]
\end{aligned}$$

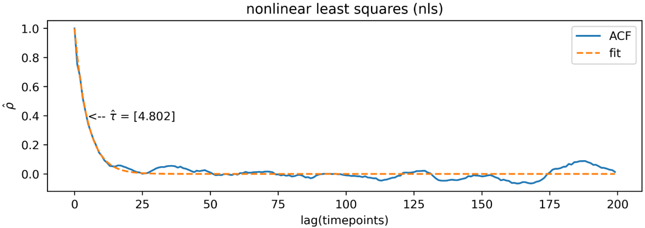
(Newey et al. 1987)

Least Squares Methods

Autoregressive Model **Linear/Ordinary Least Squares**:



Exponential Decay Model **Nonlinear Least Squares**:



Estimation of Autoregressive Model

Est: Linear Least Squares

$$\hat{\phi} = (\sum_{t=2}^{T} x_{t-1}^2)^{-1}(\sum_{t=2}^{T} x_t x_{t-1}) \tag{15}$$

$$\hat{\tau} = g(\hat{\phi}) = -\frac{1}{\log(|\hat{\phi}|)} \tag{16}$$

Est: Standard Error

$$\mathrm{se}_{\mathrm{NW}}(\hat{\phi}) = \sqrt{\hat{q}^{-1}\hat{\omega}\hat{q}^{-1}} \tag{17}$$

$$\mathrm{se}_{\mathrm{NW}}(\hat{\tau}) = \mathrm{se}_{\mathrm{NW}}(\hat{\phi})\frac{d}{d\phi}g(\hat{\phi}) \tag{18}$$

Estimation of Autoregressive Model

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$$\hat{\phi} = (\sum_{t=2}^{T} x_{t-1}^2)^{-1}(\sum_{t=2}^{T} x_t x_{t-1}) \tag{15}$$

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$$\mathrm{se}_{\mathrm{NW}}(\hat{\tau}) = \mathrm{se}_{\mathrm{NW}}(\hat{\phi})\frac{d}{d\phi}g(\hat{\phi}) \tag{18}$$

Estimation of Exponential Decay Model

Est: Autocorrelation Function

$$\hat{\rho}_k = (\hat{\gamma}_0)^{-1}(\hat{\gamma}_k) = (\sum_{t=1}^{T} x_t^2)^{-1}(\sum_{t=k+1}^{T} x_t x_{t-k}) \quad (19)$$

Est: Nonlinear Least Squares

$$\hat{S}(\phi) = \frac{1}{K}\sum_{k=1}^{K}(\hat{\rho}_k - \phi^k)^2 \quad (20)$$

$$\hat{\phi}^* = \underset{\phi}{\operatorname{argmin}}\ \hat{S}(\phi) \quad (21)$$

$$\hat{\tau}^* = g(\hat{\phi}^*) = -\frac{1}{\log(|\hat{\phi}^*|)} \quad (22)$$

Est: Standard Error

$$\mathrm{se}_{\mathrm{NW}}(\hat{\phi}) = \sqrt{\hat{q}^{-1}\hat{\omega}\hat{q}^{-1}} \quad (23)$$

$$\mathrm{se}_{\mathrm{NW}}(\hat{\tau}) = \mathrm{se}_{\mathrm{NW}}(\hat{\phi})\frac{d}{d\phi}g(\hat{\phi}) \quad (24)$$

Estimation of Exponential Decay Model

Est: Autocorrelation Function

$$\hat{\rho}_k = (\hat{\gamma}_0)^{-1}(\hat{\gamma}_k) = (\sum_{t=1}^{T} x_t^2)^{-1}(\sum_{t=k+1}^{T} x_t x_{t-k}) \tag{19}$$

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Est: Standard Error

$$\text{se}_{\text{NW}}(\hat{\phi}) = \sqrt{\hat{q}^{-1}\hat{\omega}\hat{q}^{-1}} \tag{23}$$

$$\text{se}_{\text{NW}}(\hat{\tau}) = \text{se}_{\text{NW}}(\hat{\phi})\frac{d}{d\phi}g(\hat{\phi}) \tag{24}$$

Estimation of Exponential Decay Model

Est: Autocorrelation Function

$$\hat{\rho}_k = (\hat{\gamma}_0)^{-1}(\hat{\gamma}_k) = (\sum_{t=1}^{T} x_t^2)^{-1}(\sum_{t=k+1}^{T} x_t x_{t-k}) \tag{19}$$

Est: Nonlinear Least Squares

$$\hat{S}(\phi) = \frac{1}{K}\sum_{k=1}^{K}(\hat{\rho}_k - \phi^k)^2 \tag{20}$$

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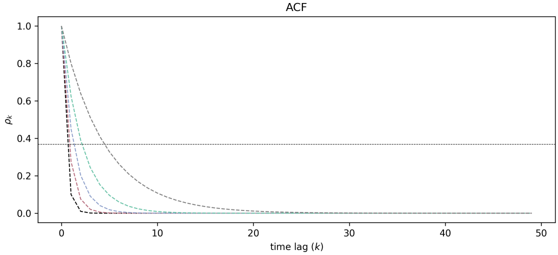
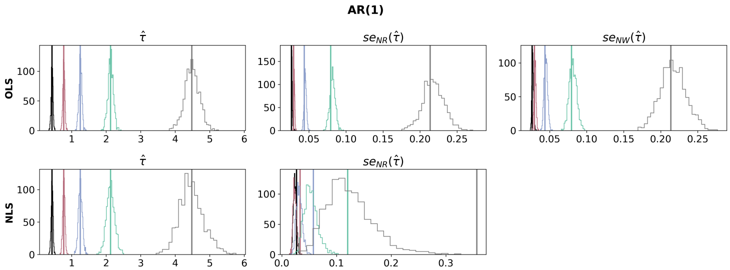
AR-1 Simulation

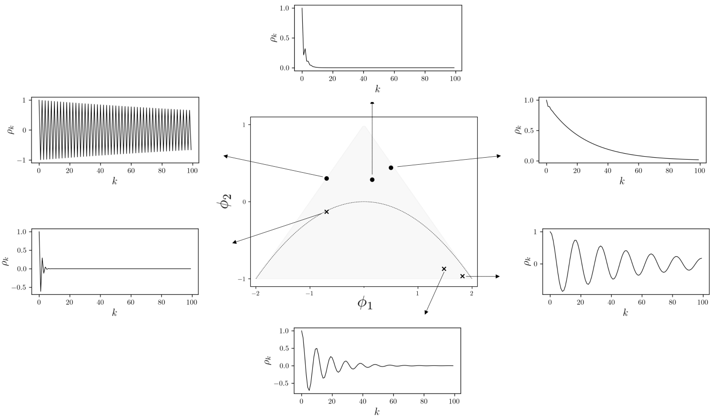
- **Setting**: $T = 4800$ timepoints, $N = 1000$ repeats.
- **AR process**: $x_t = \phi x_{t-1} + e_t, \quad e_t \overset{iid}{\sim} \mathcal{N}(0,1)$
- **Parameters**:
  $\phi \in \{0.1, 0.28, 0.45, 0.62, 0.8\}$



AR-1 Results

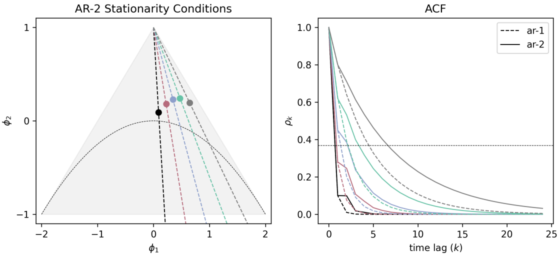


AR-2 Stationarity Conditions

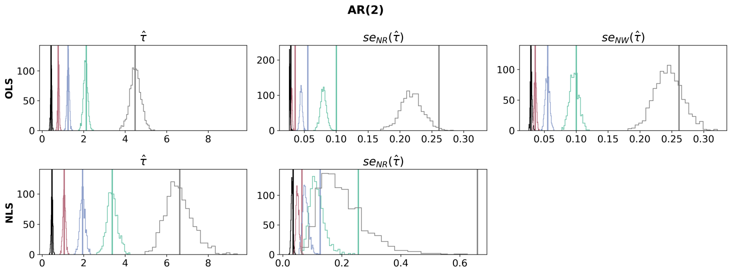


AR-2 Simulation

- **Setting**: $T = 4800$ timepoints, $N = 1000$ repeats.
- **AR process**: $x_t = \phi_1 x_{t-1} + \phi_2 x_{t-2} + e_t, \quad e_t \overset{iid}{\sim} \mathcal{N}(0,1)$
- **Parameters**:
  $[\phi_1, \phi_2] \in \{[0.1, 0.1], [0.2, 0.2], [0.4, 0.2], [0.5, 0.2], [0.7, 0.2]\}$

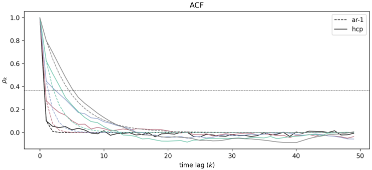


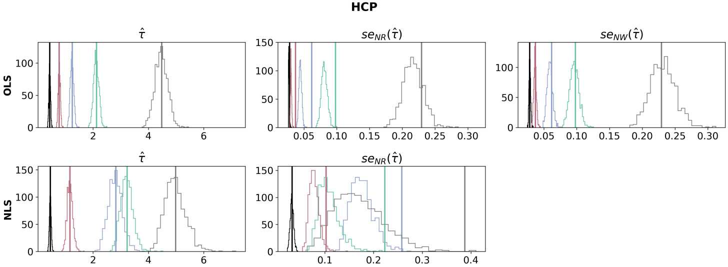
AR-2 Results



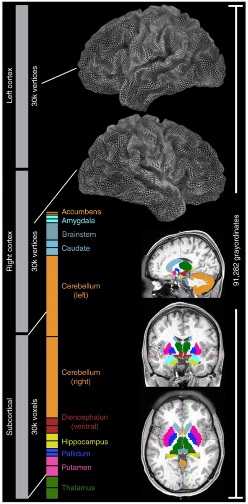
HCP Simulation

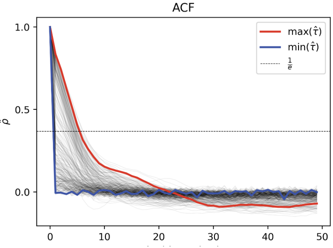
- **Setting**: $T = 4800$ timepoints, $N = 1000$ repeats.
- **Parameters**:
  Brain Region $\#\{7, 12, 126, 137, 143\}$

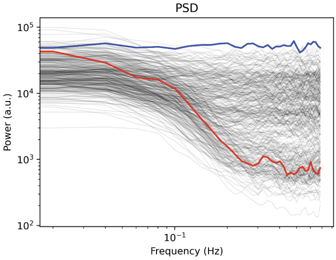




Dataset Description



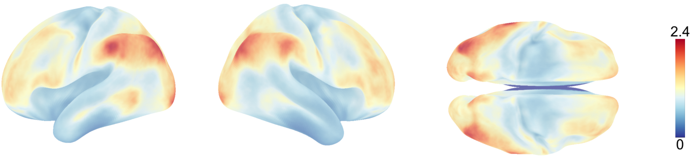




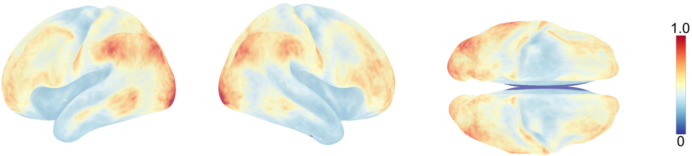
1. Developing Methods: 10 subjects, 4800 timepoints, 300 regions
2. **Estimating Maps: 184 subjects, 3600 timepoints, 91282 grayordinates**

Timescale Maps

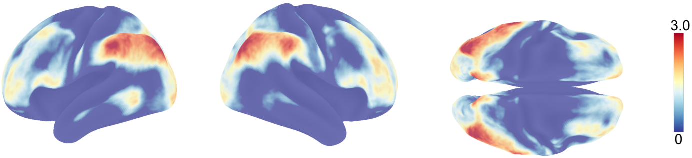
$\hat{\tau}_{OLS}$



$\mathrm{se}_{NW}(\hat{\tau})$



$(\hat{\tau}_{OLS} - 1)/\mathrm{se}_{NW}(\hat{\tau})$



Conclusions and Future Directions

Conclusions:

- Timescales (and their standard errors) can be accurately estimated, even if the models are misspecified
- Autoregressive models provide a computationally efficient alternative to exponential decay models
- The choice between the two depends on the trade off between dense sampling in time versus space

Future Directions:

- Group-level models
- Nonstationary timeseries (autocorrelations that are time dependent)
- Multivariate settings (vector autoregession)

Acknowledgments

Prof. Armin Schwartzman, Prof. Bradley Voytek, Dr. Samuel Davenport

References:
Papers:
github.com/griegner/fmri-timescales/latex/zotero.bib

Code:
github.com/griegner/fmri-timescales

Properties of OLS

Consistency: by the Ergodic and Continuous Mapping Theorems, the coefficients of an AR-1 model can be consistently estimated, as $T \to \infty$

$$\hat{\phi} = (\frac{1}{T}\sum_{t=2}^{T} x_{t-1}^2)^{-1}(\frac{1}{T}\sum_{t=2}^{T} x_t x_{t-1}) \underset{p}{\to} (\mathbb{E}[X_{t-1}^2])^{-1}(\mathbb{E}[X_t X_{t-1}]) = \phi \tag{25}$$

Similarly:

$$\hat{\omega} \underset{p}{\to} \omega \tag{26}$$

Limiting variance: as $T \to \infty$ we can approximate the asymptotic variance of ϕ and τ using a CLT for correlated observations (Hansen 2022).

$$\frac{\hat{\phi} - \phi}{\text{se}_{NW}(\hat{\phi})} \underset{d}{\to} \mathcal{N}(0,1) \tag{27}$$

$$\frac{\hat{\tau} - \tau}{\text{se}_{NW}(\hat{\phi}) \cdot \frac{d}{d\phi}(\hat{\phi})} \underset{d}{\to} \mathcal{N}(0,1) \tag{28}$$

Properties of OLS

Consistency: by the Ergodic and Continuous Mapping Theorems, the coefficients of an AR-1 model can be consistently estimated, as $T \to \infty$

$$\hat{\phi} = (\frac{1}{T}\sum_{t=2}^{T} x_{t-1}^2)^{-1}(\frac{1}{T}\sum_{t=2}^{T} x_t x_{t-1}) \underset{p}{\to} (\mathbb{E}[X_{t-1}^2])^{-1}(\mathbb{E}[X_t X_{t-1}]) = \phi \tag{25}$$

Similarly:

$$\hat{\omega} \underset{p}{\to} \omega \tag{26}$$

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$$\frac{\hat{\phi} - \phi}{\mathrm{se}_{NW}(\hat{\phi})} \underset{d}{\to} \mathcal{N}(0,1) \tag{27}$$

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Properties of NLS

Consistency: if the minimizer ϕ^k is unique, $S(\phi) > S(\phi^*)$ for all $\phi \neq \phi^*$, then as $K \to \infty$

$$\hat{\phi}^* \underset{p}{\to} \phi^* \tag{29}$$

And under (??):

$$\hat{\omega} \underset{p}{\to} \omega \tag{30}$$

Limiting Variance: as $K \to \infty$ we can approximate the asymptotic variance of ϕ and τ using a CLT for correlated observations (Hansen 2022).

$$\frac{\hat{\phi}^* - \phi^*}{\mathrm{se}_{NW}(\hat{\phi}^*)} \underset{d}{\to} \mathcal{N}(0,1) \tag{31}$$

$$\frac{\hat{\tau}^* - \tau^*}{\mathrm{se}_{NW}(\hat{\phi}^*) \cdot \frac{d}{d\phi} g(\phi^*)} \underset{d}{\to} \mathcal{N}(0,1) \tag{32}$$

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