Green Fine Tuning for Molecular Property Prediction

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Outline

Business Understanding

Context and Motivation

- **Context**: Rise of Deep Learning in Drug Discovery (Transformers, GNNs).
- **Problem**: "Red AI" trend leading to high computational costs and energy consumption.
- **Solution**: **Green AI** paradigm - sustainable AI.
- **Alignment**: UN 2030 Agenda for Sustainable Development.
  - Goal 12: Responsible Consumption and Production.
  - Goal 13: Climate Action.

Business Objectives

Primary Goal

Demonstrate that sustainable practices can be integrated into molecular property prediction pipelines without significant loss in performance.

- **Sustainability**: Drastically reduce CO_2eq emissions during fine-tuning.
- **Reliability**: Maintain predictive accuracy for real-world use.

Expectations

- CO_2 reduction: 20% - 50%.
- Performance margin: Within 10% of traditional methods.

Data Understanding

Datasets (MoleculeNet)

Classification Tasks:

- **HIV**: Predict if HIV is active or inactive.
- **BACE**: Predict inhibitors of BACE-1 enzyme (Alzheimer's).
- **BBBP**: Predict blood-brain barrier penetration.

Regression Tasks:

- **Lipophilicity**: Predict octanol/water distribution coefficient.
- **Malaria**: Predict inhibition of malaria parasite growth.
- **CEP**: Predict efficiency of organic photovoltaic molecules.

Dataset Details

Dataset	Task	Key Components	Rows
BACE	Classification	mol, CID, Class, pIC50	1,513
BBBP	Classification	num, name, p_np, smiles	2,050
HIV	Classification	smiles, activity	41,126
CEP	Regression	smiles, PCE	29,978
Malaria	Regression	smiles, activity	9,999
Lipophilicity	Regression	CMPD_CHEMBLID, exp, smiles	4,200

Data Representation: SMILES

SMILES (Simplified Molecular Input Line Entry System):

- ASCII strings representing chemical structures.
- **Atoms**: C, N, O, etc. (Upper: aliphatic, Lower: aromatic).
- **Bonds**: Single (implicit), Double (=), Triple (#).
- **Branching**: Parentheses ().
- **Rings**: Numbers (e.g., C1CCCCC1).

Crucial for converting 3D structures into 1D sequences for Transformers or Graphs for GNNs.

Data Preparation

Preprocessing Pipeline

1. **SMILES Validation**:
   - **Parsing**: Check syntax errors using RDKit.
   - **Sanitization**: Valence checks, Kekulization, Aromaticity detection.
2. **Data Variants**:
   - **Transformer Variant**: SMILES string + Target label.
   - **Graph Variant**: Molecular graphs generated from SMILES.

Graph Generation (for GNNs)

Conversion of SMILES to Graph $G = (V, E)$ using RDKit.

Node Features (V):

- Atomic Number
- Chirality
- Degree
- Formal Charge
- Hybridization
- Aromaticity

Edge Features (E):

- Bond Type
- Stereochemistry
- Conjugation

Serialized as PyTorch Geometric `Data` objects (.pt files).

Modeling

Architectures

Sequence-based (Transformers)

- Input: SMILES strings.
- Models:
  - ChemBERTa
  - ChemBERTa-2
  - SELFormer
  - SMILES-BERT

Graph-based (GNNs)

- Input: Molecular Graphs.
- Model:
  - **GraphMAE**: Masked Autoencoder approach for self-supervised learning.

Green FineTuning (GFT) Strategy

Core Idea: Stop training when marginal performance gain doesn't justify energy cost.

Instantaneous GFT Ratio

$$GFT_t = \frac{\Delta P_t}{\Delta E_t} = \frac{Perf_t - Perf_{t-1}}{Emission_t - Emission_{t-1}}$$

where:

- ΔP_t = improvement in validation metric at epoch t
- ΔE_t = incremental CO_2eq emitted during epoch t

Smoothed Trend (EMA)

To stabilize the volatile instantaneous efficiency:

$$S_t = \alpha\, GFT_t + (1 - \alpha)\, S_{t-1}$$

where $\alpha = 0.9$. Initialization: $S_0 = GFT_0$ (or 0).

GFT Stopping Rule

Stopping Condition

Training stops when instantaneous efficiency falls below the smoothed trend:

$$\text{Stop if } GFT_t < \beta \cdot S_t$$

where $\beta = 0.2$ is the tolerance factor.

Implementation Details

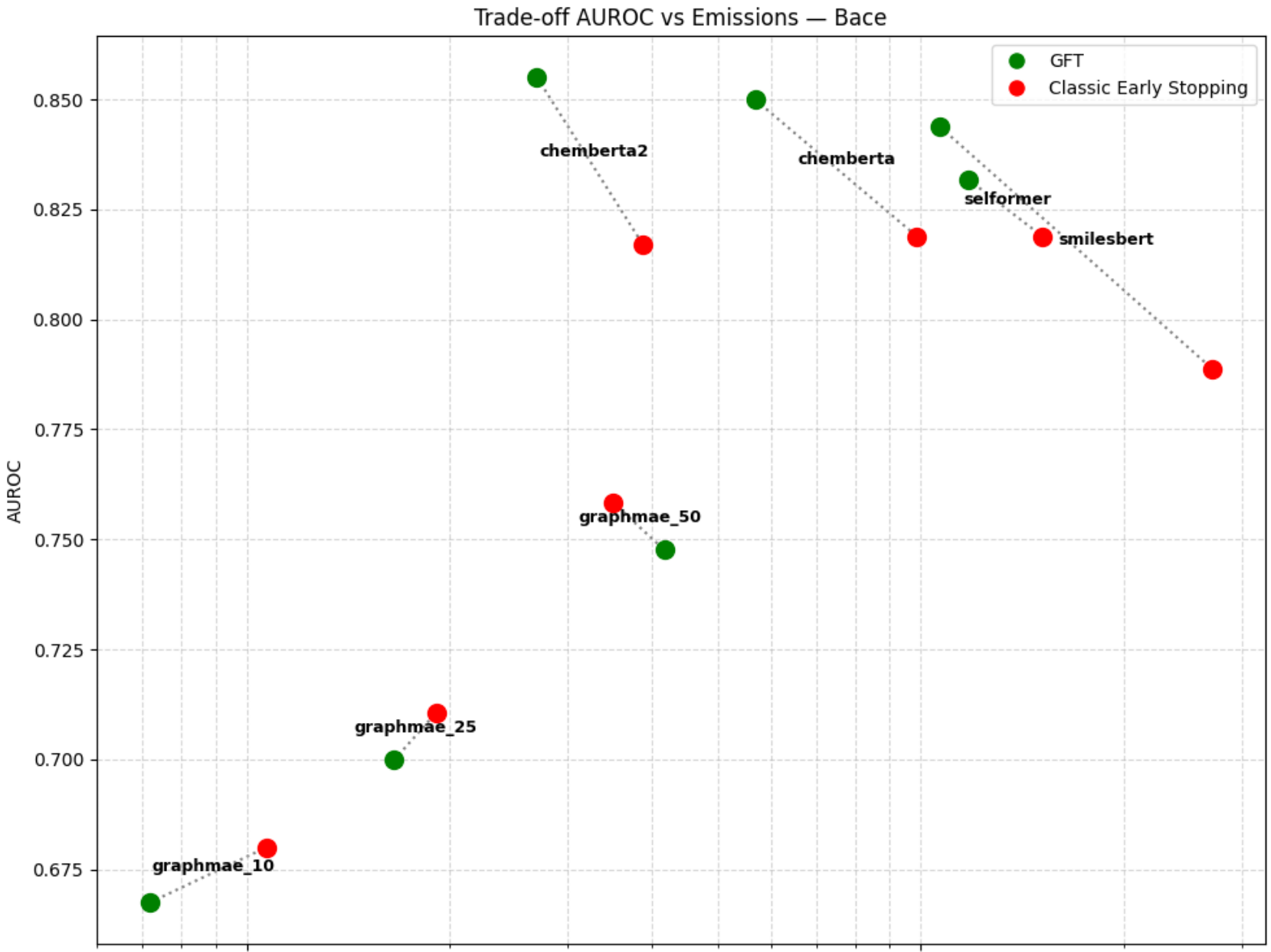
- $Perf_t$ is the validation metric:
  - ROC-AUC for classification tasks
  - Negative RMSE for regression tasks
- Warmup period: 3 epochs (Transformers), variable for GraphMAE
- Energy tracking: CodeCarbon library

Evaluation

Results: Classification Tasks

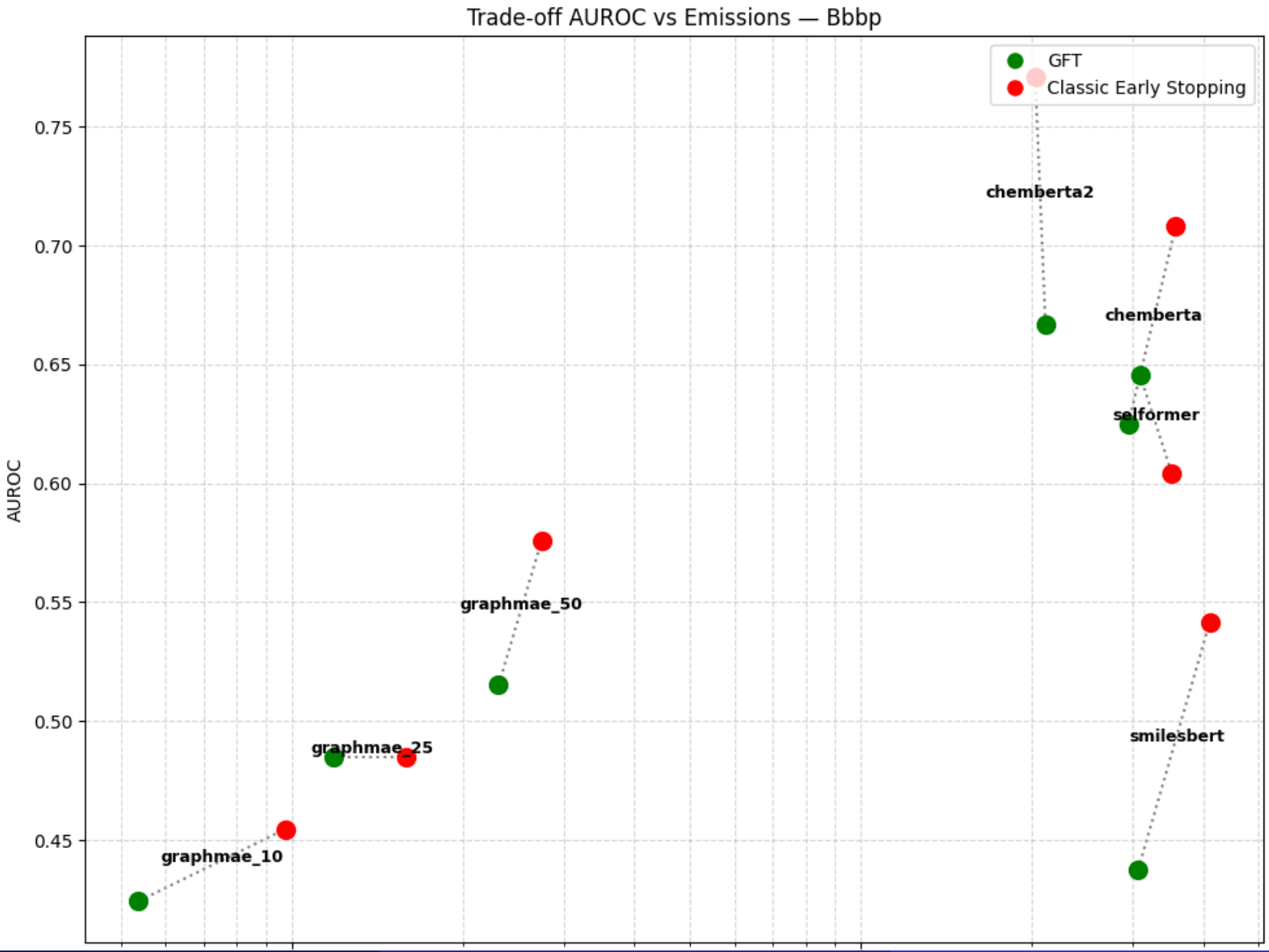
- **BACE**:
  - Transformers: +1.6% to +7.0% performance, -22% to -60% emissions.
  - Early stopping prevents overfitting.
- **HIV**:
  - Strong improvements (e.g., SELFormer +16.2% perf, -44% emissions).
  - ChemBERTa-2: Stable perf, -60.6% emissions.
- **BBBP**:
  - Mixed results. Some models degrade (ChemBERTa -11.8%).
  - SELFormer resilient (+6.9% perf).

Trade-off: BACE



Trade-off: HIV

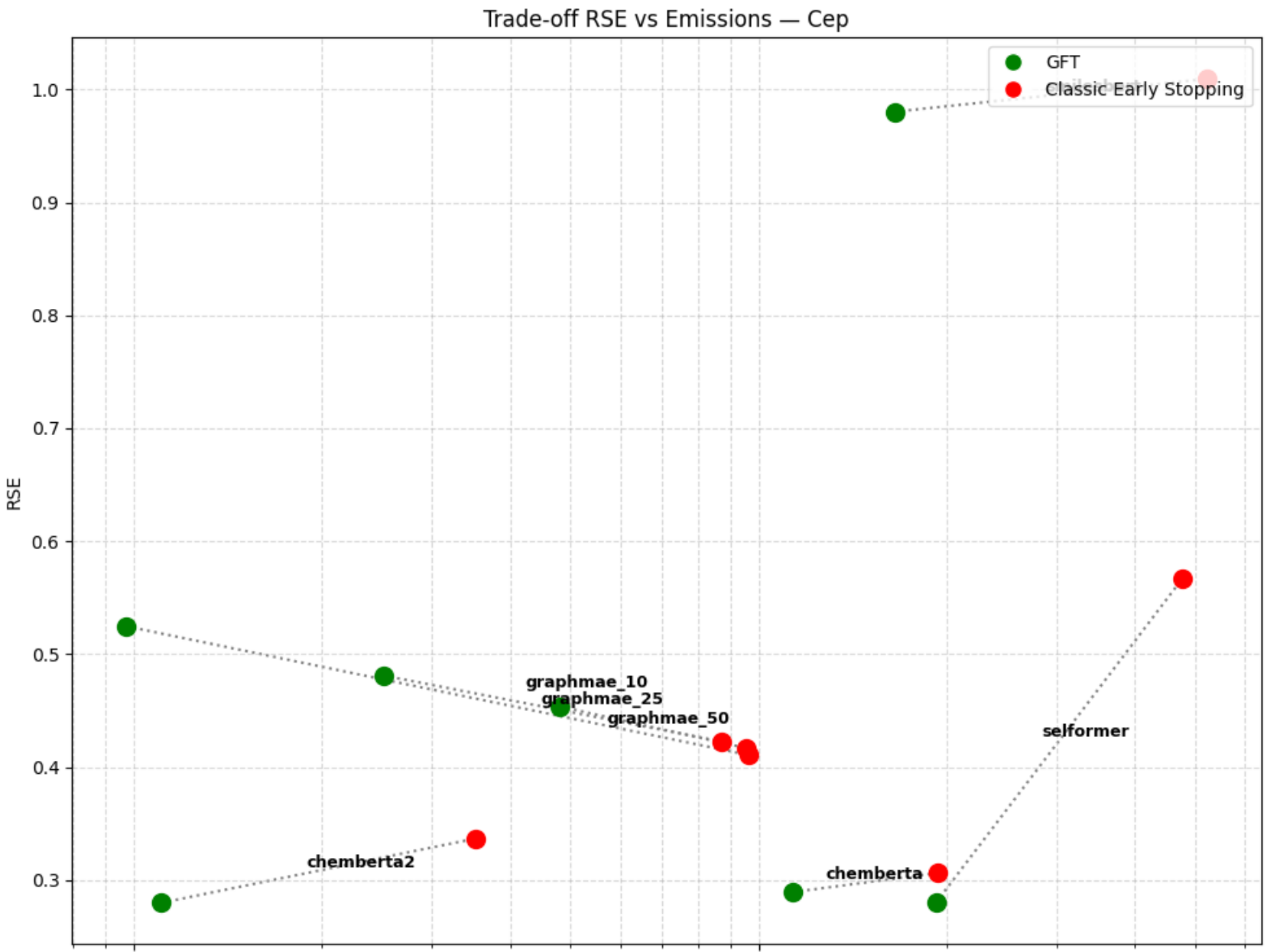
Trade-off: BBBP



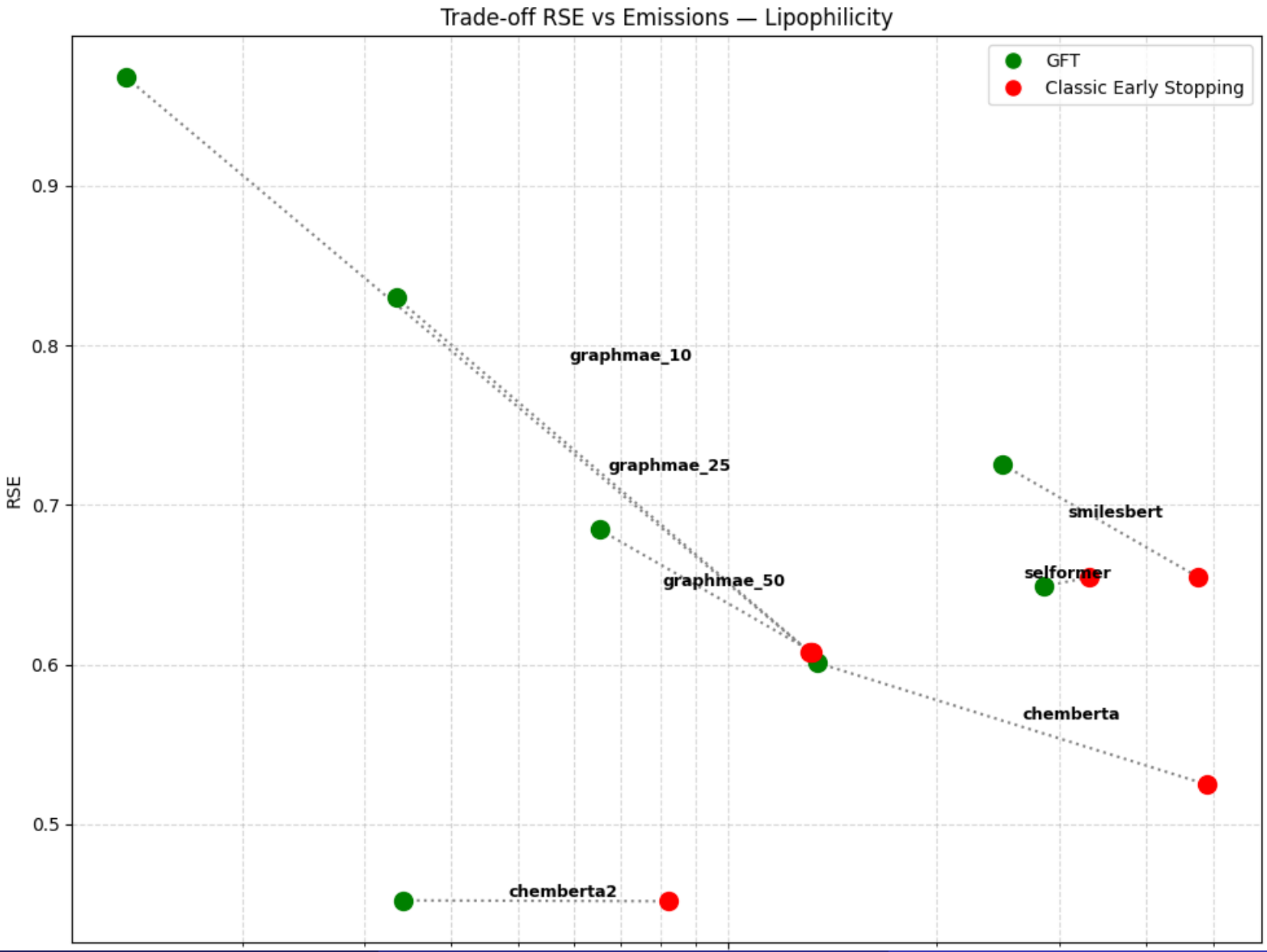
Results: Regression Tasks

- **CEP**:
  - Excellent results. SELFormer: +50.6% perf, -59.7% emissions.
  - GraphMAE: Trade-off between warmup and performance.
- **Lipophilicity**:
  - Most challenging. Many models degrade.
  - Requires extended fine-tuning.
- **Malaria**:
  - Moderate success. ChemBERTa-2: +3.3% perf, -23.6% emissions.
  - GraphMAE benefits from longer warmup.

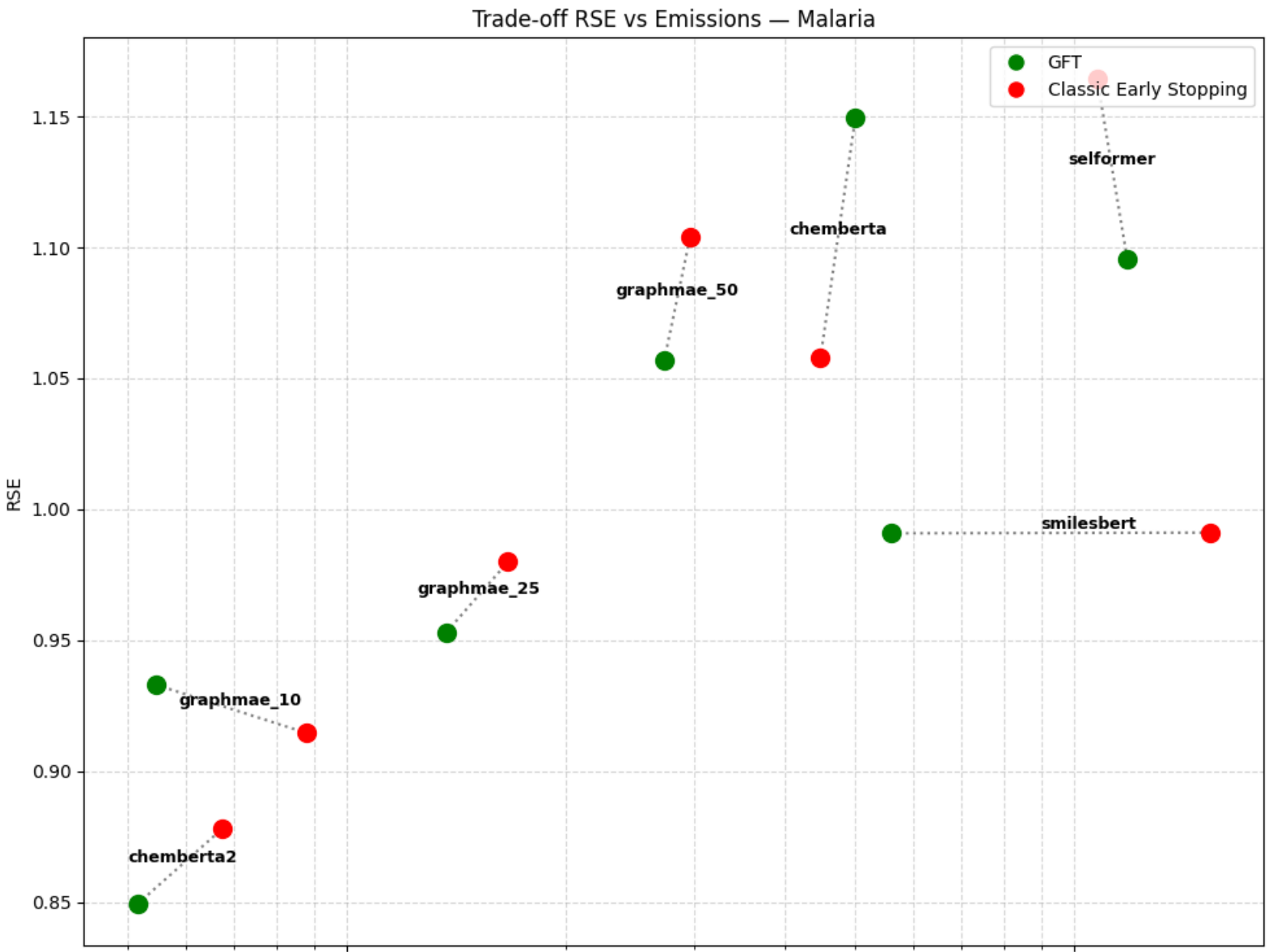
Trade-off: CEP



Trade-off: Lipophilicity



Trade-off: Malaria

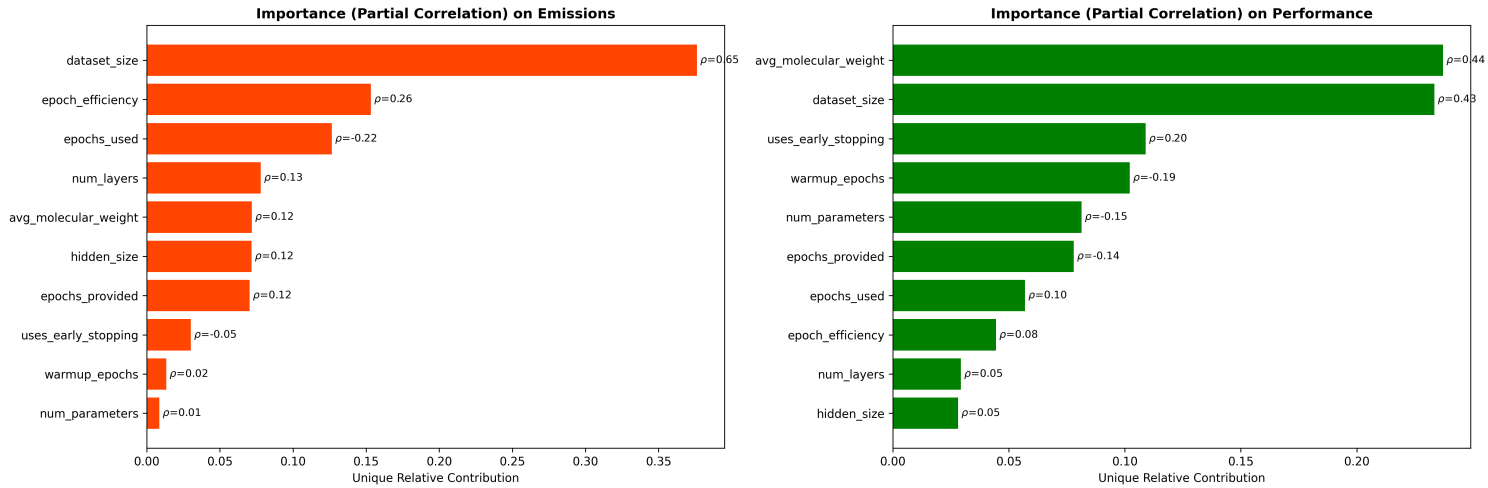


Explainability Analysis

- **Motivation**: understand which factors drive emissions and performance to improve GFT.
- Use **Partial Correlation** to isolate each feature's unique contribution while controlling for others.
- Valuable when features are collinear across experiments.

Factors Influencing Emissions

- **Top drivers**: Dataset Size ($\rho = 0.65$), Epoch Efficiency ($\rho = 0.26$).
- **Interactions**: Epochs Used shows interaction effects with dataset size and efficiency.
- **Model architecture**: moderate influence (num_layers, hidden_size, $\rho \approx 0.12$).
- **Early stopping**: minimal direct effect ($\rho = -0.05$) its benefit is mediated by fewer epochs used.



Conclusions

Key Findings

- **GFT Effectiveness**: Drastic emission reductions (60%-80%) often possible with maintained or improved accuracy.
- **Classification vs Regression**:
  - Classification: Often "win-win" (prevents overfitting).
  - Regression: Clearer trade-off, requires careful tuning.
- **Explainability Insights**:
  - **Dataset Size**: Dominant factor for emissions.
  - **Early Stopping**: Positively correlates with performance.

Recommendations

1. **Implement GFT**: Standardize adaptive early stopping.
2. **Optimize Dataset Usage**: Focus on data quality over quantity.
3. **Task-Specific Tuning**: Adjust warmup epochs based on task complexity (especially for Regression/GNNs).
4. **Model Selection**: Transformers show high resilience in classification tasks.

Thank You!