MurreNet: Modeling Holistic Multimodal Representations Between Histopathology and Genomic Profiles for Survival Prediction

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Motivations

(1) Multimodal features often contain **overlapping and redundant information** that will hinder reliable fusion, making it challenging to identify complementary information across modalities.

(2) Disentangled features are insufficient without proper guidance, may still **lack semantic structure**, posing a challenge to effective **meaningful alignment across feature spaces**.

(3) Simple feature fusion **overlook the hierarchical and intricate dependencies** between heterogeneous modalities, leading to suboptimal cross-modality representation learning.

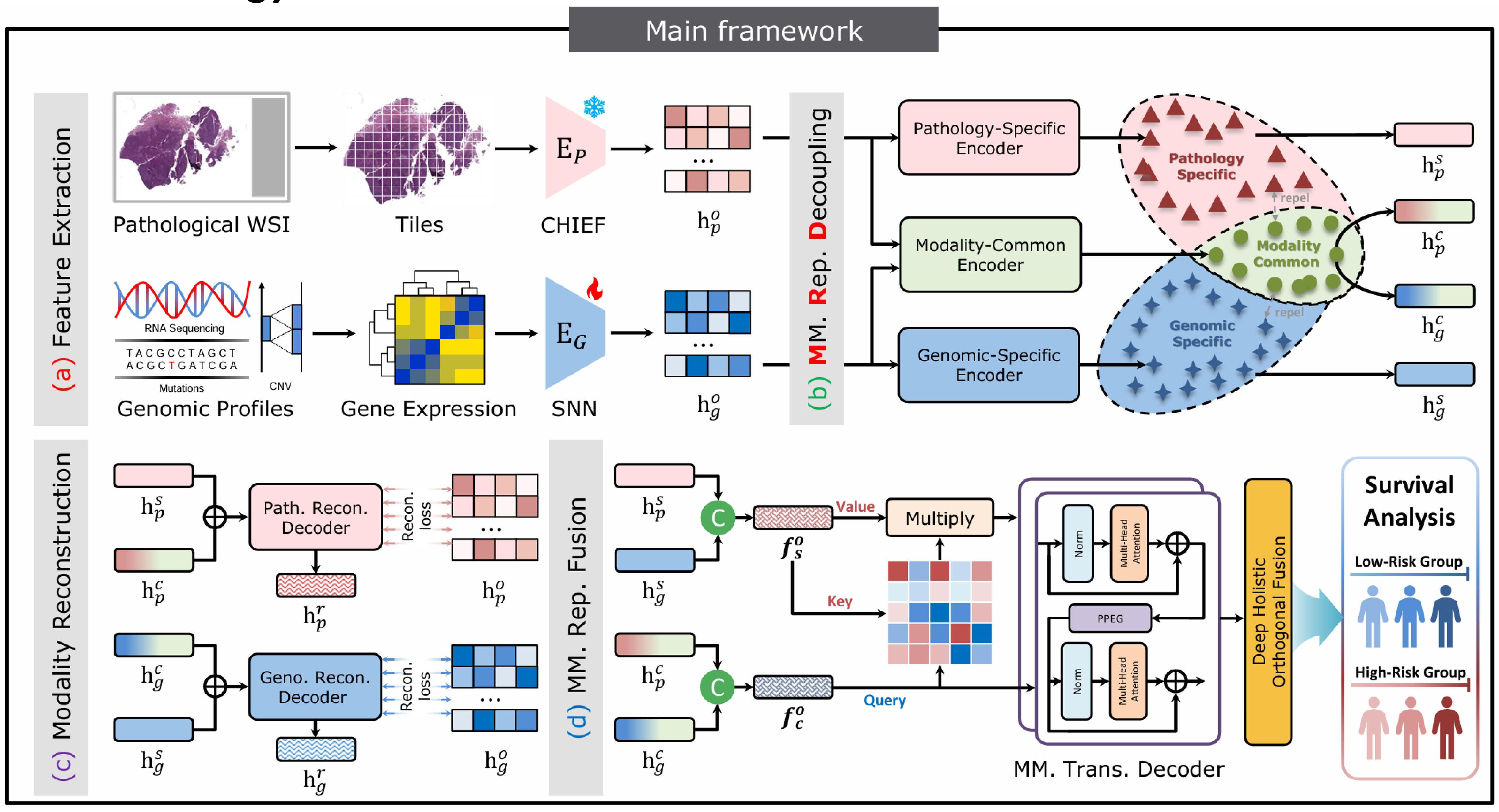
Contributions

(1) **M**ultimodal **R**epresentation **D**ecomposition module (**MRD**) is present to **explicitly decompose input data into modality-specific and -shared representations**, thereby reducing redundancy between modalities.

(2) A novel regularization strategy is designed to impose constraints on **distribution similarity, difference**, and **representativeness** of the disentangled modality representations.

(3) **D**eep **H**olistic **O**rthogonal **F**usion (**DHOF**) is proposed to integrate the modality-specific and -common representations for modeling **holistic interactions across heterogenous modalities**.

Methodology



Multimodal Representation Decoupling

(1) Extract specific representations via modality-specific encoders (2-Linear-layer MLP):

$$\mathrm{h}_p^s, \mathrm{h}_g^s = \mathrm{MLP}(\mathrm{h}_p^o), \mathrm{MLP}(\mathrm{h}_g^o)$$

(2) Calculates multimodal co-attention matrix:

$$\mathbb{A} = \mathrm{Linear}(\mathrm{h}_p^o)^\top \cdot \mathrm{Linear}(\mathrm{h}_g^o),$$

(3) Generate modality-common representations via modality-common encoder Γ_c :

$$\mathrm{h}_p^c = \Gamma_c(\mathrm{h}_p^o, \mathrm{h}_g^o) = \mathrm{MLP}(\mathbb{A}^\top) * \mathrm{h}_p^o,$$

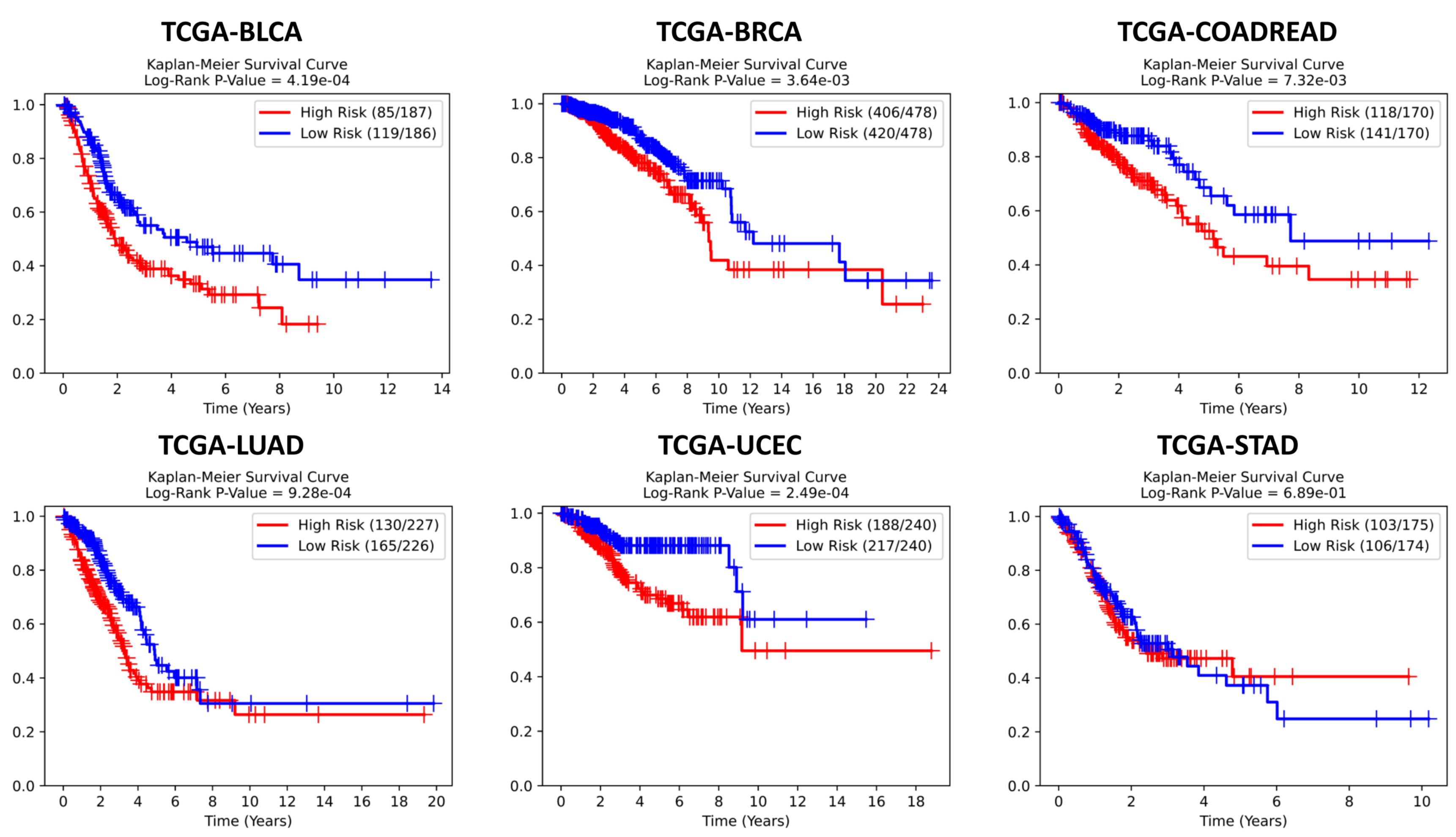
$$\mathrm{h}_g^c = \Gamma_c(\mathrm{h}_p^o, \mathrm{h}_g^o) = \mathrm{MLP}(\mathbb{A}) * \mathrm{h}_g^o,$$

Results & Analysis

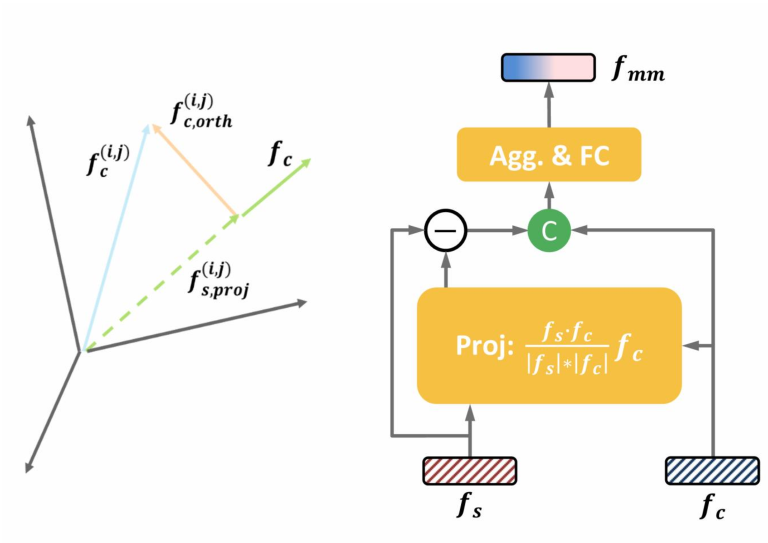
Comparison with SOTAs for Survival Prediction

Methods	Modality P.	Modality G.	BLCA ($n = 373$)	BRCA ($n = 956$)	COADREAD ($n = 340$)	LUAD ($n = 453$)	UCEC ($n = 480$)	STAD ($n = 349$)
MLP		✓	0.611 ± 0.030	0.619 ± 0.053	0.675 ± 0.049	0.619 ± 0.044	0.675 ± 0.069	0.607 ± 0.045
SNN [11]		✓	0.625 ± 0.054	0.621 ± 0.051	0.606 ± 0.087	0.615 ± 0.044	0.703 ± 0.072	0.603 ± 0.052
Coxnet [7]		✓	0.591 ± 0.061	0.593 ± 0.067	0.601 ± 0.059	0.605 ± 0.044	0.535 ± 0.051	0.523 ± 0.055
ABMIL [8]	✓		0.640 ± 0.032	0.642 ± 0.030	0.703 ± 0.064	0.607 ± 0.041	0.701 ± 0.038	<u>0.638 ± 0.028</u>
DSMIL [13]	✓		0.636 ± 0.031	0.657 ± 0.037	0.684 ± 0.071	0.591 ± 0.026	0.729 ± 0.063	0.630 ± 0.032
CLAM [19]	✓		0.618 ± 0.042	0.593 ± 0.077	0.643 ± 0.108	0.580 ± 0.029	0.647 ± 0.037	0.634 ± 0.054
TransMIL [20]	✓		0.640 ± 0.039	0.590 ± 0.058	0.684 ± 0.024	0.592 ± 0.048	0.705 ± 0.027	0.604 ± 0.054
DTFD-MIL [28]	✓		0.610 ± 0.025	0.625 ± 0.060	0.633 ± 0.061	0.590 ± 0.033	0.663 ± 0.016	0.580 ± 0.033
M3IF [14]	✓	✓	0.662 ± 0.043	0.639 ± 0.062	<u>0.710 ± 0.043</u>	0.628 ± 0.050	0.724 ± 0.103	0.607 ± 0.044
MCAT [5]	✓	✓	0.677 ± 0.062	<u>0.691 ± 0.041</u>	0.649 ± 0.052	0.675 ± 0.039	0.658 ± 0.055	0.586 ± 0.027
CMTA [30]	✓	✓	0.683 ± 0.016	0.667 ± 0.033	0.678 ± 0.040	0.648 ± 0.036	0.740 ± 0.066	0.584 ± 0.023
MoME [25]	✓	✓	0.650 ± 0.033	0.659 ± 0.032	0.692 ± 0.038	0.650 ± 0.024	0.705 ± 0.041	0.630 ± 0.039
MOTCat [26]	✓	✓	<u>0.683 ± 0.025</u>	0.675 ± 0.021	0.618 ± 0.030	0.667 ± 0.027	0.685 ± 0.052	0.596 ± 0.028
SurvPath [9]	✓	✓	0.673 ± 0.011	0.685 ± 0.024	0.650 ± 0.024	<u>0.676 ± 0.036</u>	0.737 ± 0.049	0.622 ± 0.045
PORPOISE [6]	✓	✓	0.651 ± 0.046	0.624 ± 0.048	0.702 ± 0.045	0.642 ± 0.042	<u>0.737 ± 0.097</u>	0.612 ± 0.038
MurreNet	✓	✓	**0.710 ± 0.030**	**0.718 ± 0.016**	**0.725 ± 0.044**	**0.691 ± 0.040**	**0.752 ± 0.075**	**0.651 ± 0.062**

Kaplan-Meier Survival Curves



Deep Holistic Orthogonal Fusion



(1) Calculates the projection $f_{s,proj}^{(i,j)}$ of each feature in specific representation onto the common representation f_c:

$$f_{s,orth}^{(i,j)} = f_s^{(i,j)} - f_{s,proj}^{(i,j)},$$

(2) Compute orthogonal component:

$$f_{s,proj}^{(i,j)} = \frac{\sum_{k=1}^{K} f_{s,k}^{(i,j)} \cdot f_{c,k}}{\sum_{k=1}^{K} (f_{c,k})^2} \cdot f_c$$

Training Objectives

$$\mathcal{L}_{total} = \alpha \mathcal{L}_{sim} + \beta \mathcal{L}_{diff} + \gamma \mathcal{L}_{recon} + \mathcal{L}_{surv}$$

$$\mathcal{L}_{sim} = \mathcal{L}_1(\mathrm{h}_p^o, \mathrm{h}_p^c) = \frac{1}{n} \left\| \mathrm{h}_p^o - \mathrm{h}_p^c \right\|_1 \quad (\alpha = \beta = 1 \times 10^{-4}, \gamma = 1)$$

$$\mathcal{L}_{diff} = \mathcal{D}_{KL}(\mathrm{h}_p^c, \mathrm{h}_p^s) + \mathcal{D}_{KL}(\mathrm{h}_g^c, \mathrm{h}_g^s) = \sum_m^{\{p,g\}} \left[\mathrm{h}_m^c \cdot \log(\frac{\mathrm{h}_m^c}{\mathrm{h}_m^s}) \right]$$

$$\mathcal{L}_{recon} = \frac{1}{2} \left(\mathcal{L}_{MSE}(\mathrm{h}_p^o, \mathrm{h}_p^r) + \mathcal{L}_{MSE}(\mathrm{h}_g^o, \mathrm{h}_g^r) \right) = \frac{1}{2} \sum_m^{\{p,g\}} (\mathrm{h}_m^o - \mathrm{h}_m^r)^2$$

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