Turk. J. Math. Comput. Sci.
18(3)(2026) 918–925
© MatDer
DOI : 10.47000/tjmcs.1834256

An Application of the Bipolar Metric Space Structure for Missing Data Imputation in Ligand–Target Interactions

Utku Gürdal[1,*], Selim Çetin[1], Reha Yapali[2]

[1]*Department of Mathematics, Faculty of Sciences & Humanities, Burdur Mehmet Akif Ersoy University, Burdur, Türkiye.*
[2]*Department of Mathematics, Faculty of Sciences & Humanities, Muş Alparslan University, Muş, Türkiye.*

Received: 02-12-2025 • Accepted: 26-04-2026

Abstract. In this study, the bipolar metric space structure is tested on a real dataset for the first time. In this context, ligand–target interaction scores are examined and transformed into a form compatible with the bipolar metric function, an incomplete-data scenario is evaluated, and in addition, the closest pairs of the same type are identified and the resulting findings are analyzed. The model is also applied to provide theoretical estimations for some missing entries in the dataset. By emphasizing that the proposed method can be tested in various contexts across the natural sciences and the humanities, the study thus presents an initial example in this direction.

2020 AMS Classification: 54E35, 62H12, 62J99, 62P10, 92C42.

Keywords: Bipolar metric space, missing data imputation, ligand target interaction.

1. Introduction

Bipolar metric spaces are among the most recent components of the expansion process of the metric space concept, which has accelerated in the 21st century. In most variations of metric spaces, some axioms, particularly the triangle inequality, have been modified in various ways, or, for example, the range of values that the metric function can take has been extended. Most of these models aim to generalize metric spaces and have produced both analytical and topological results.

In this context, the bipolar metric approach proposed by Mutlu and Gürdal in 2016 possesses a remarkable distinction, as the distance function is defined not between elements of a single set but between two separate conceptual sets. In such structures, the distance between two points belonging to the same set may be meaningless or non-measurable, while the only meaningful distance is the one between points selected from two distinct sets.

The fundamental axioms on which this approach is based correspond exactly to the classical metric conditions at the intersection of these two sets, called poles. However, a bipolar metric d defined on a pair of sets (X, Y) satisfies an inequality in which four points play a role, two from each pole. This condition, known as the quadrilateral inequality,

$$d(x, y) \leq d(x, y') + d(x', y') + d(x', y)$$

is valid for all $x, x' \in X$ and $y, y' \in Y$. In other words, the cost of moving directly from an element $x \in X$ to an element $y \in Y$ cannot exceed the total cost of a transition performed through two intermediate points. This inequality bears a structural similarity to rectangular metric spaces, yet it is more natural in the sense that it does not require the

*Corresponding Author
Email addresses: utkugurdal@gmail.com (U. Gürdal), seliimcetin@gmail.com (S. Çetin), reha.yapali@alparslan.edu.tr (R. Yapalı)

intermediate points to be distinct from the original ones, and it exhibits a unique geometric behavior due to its reliance on two separate sets.

Since its introduction [25], bipolar metric spaces have been studied primarily within the framework of the fixed point theory [8, 14, 19, 21, 24, 26, 27, 30, 31, 34, 41, 44, 45], and only rarely from a topological point of view [15]. They have also been applied to solving certain classes of equations [22, 29]. Moreover, numerous variants have already appeared in the literature, such as bipolar b-metric space [23, 37], bipolar b-multiplicative metric space [33], bipolar Menger probabilistic b-metric space [11], bipolar p-metric space [20], bipolar parametric metric space [6], F-bipolar metric space [35], fuzzy bipolar metric space [5, 43], generalized fuzzy bipolar metric space [17], multiplicative cone bipolar metric space [32], neutrosophic bipolar fuzzy metric space [13], triple-composed bipolar metric space [39], $\aleph$-extended fuzzy bipolar b-metric space [18], and so on.

By the 10th year of the theory, applications of bipolar metric spaces have remained mostly within a mathematical context, typically relying on the theoretical strength of metric spaces, yet they have not been tested in interdisciplinary real-life scenarios. However, as suggested in the original introductory paper [25], bipolar metric spaces provide a distinctive framework, largely stemming from the quadrilateral inequality, for modeling interactions between two different groups. The intensity of radiation between a planet and a star, the reaction rate between an acid and a base, or the performance score of a child in an activity can all be modeled in terms of distance and thus treated within the bipolar metric context. If the subject of application is observed to conform well to the ideal structure of the bipolar metric, then a potential model and method emerge for various applications, including missing data imputation.

Hypothetically, some scenarios in which the usefulness of the bipolar metric space structure appears likely to be tested include, but are not limited to, the following: reaction rates between acids and bases [4], ligand–receptor binding affinities [1], enzyme–substrate interactions [7], antibody–antigen affinities [28], compatibility between species and habitats [12], plant–nutrient absorption rates [38], drug–target cell effectiveness measures [9], the apparent brightness of stars as seen from planets [36], countries' scores on socioeconomic indicators [3], the distance between political parties and voters [10], customers' relationships with preferences [42], performance relations between a group of students and their courses [2], and the behavioral characteristics or aptitude tendencies of a group of children [16].

Modeling in these areas would also make it possible, through the inner-pseudo metrics provided in [25], to define a distance among elements of the same type; for example, questions such as which socioeconomic indicators are closer to each other or which children are more similar to one another could be answered using a metric-like function.

Testing the bipolar metric space structure in such models essentially means determining the extent to which the quadrilateral inequality fits the data. Since raw data must be processed in a way that can be interpreted as distance, the choice of the transformation function to be used here also provides an opportunity that can be exploited in favor of the bipolar metric structure. Moreover, in addition to the percentage of cases in which the quadrilateral inequality holds, the magnitude of deviation in the cases where it does not hold may also be an important factor.

While the current study uses the quadrilateral inequality mostly throughout, it should be noted that the choice is by no means arbitrary, being tightly bound to the nature of the bipolar metric spaces themselves. Specifically, the quadrilateral inequality defines the properties of bipolar metric spaces as the main axiom, and represents the connection between two separate sets. The use of this inequality makes it natural to consider the model as being within the bipolar metric space paradigm, and not as an independent and separated condition.

It should be noted that the bipartite character of the ligand-target interaction problem is reflected in the fact that all measurements between the elements are performed only when considering two separate types. The bipolar metric spaces are precisely formulated to reflect these kinds of relations, and hence are suitable for the data considered. Secondly, it should be stated that some of the objects considered, namely the induced inner pseudo-metric d_X and d_Y, are part of the bipolar metric framework. Therefore, the construction of the model without any mention of the corresponding theory does not make sense in view of the already established research. Thirdly, it is important to mention that the notion of bipolar metric spaces comes with additional mathematical structures, such as sided neighborhoods, convergence, and the corresponding topological structures.

In this context, it is of interest to determine in which fields bipolar metric modeling will perform more successfully. Since it is not feasible to test all the aforementioned fields individually within this study, one representative dataset from the natural sciences is examined here, leaving the investigation of other fields to future researchers.

As a result of this study, it has been observed that bipolar metric modeling can provide a structural and analytical tool for missing data imputation. This method carries a notable potential for innovation, particularly in areas where measurements are partially missing. While fundamental questions such as the rate at which the quadrilateral inequality

is satisfied, data consistency, the selection of suitable distance transformations, the topological implications of bipolarity, missing data imputation capacities, and methods of learning optimal distances from data remain entirely open, the present work takes a pioneering step toward revealing that bipolar metric spaces may possess a broad, previously unused range of potential applications. This unexplored domain is expected to offer an important research direction both mathematically and within the applied sciences, thereby adding a new and rich dimension to the concept of bipolar metric spaces as the theory enters its 10th year.

2. Model and Method

All mathematical operations and processing data operations were done using Python. As for our data, we downloaded the KIBA dataset from an open data source from Kaggle and took into consideration a submatrix with the largest possible amount of data recorded were included. All mathematical operations were done accordingly to the described algorithm.

The concept of a bipolar metric, introduced by Mutlu and Gürdal in 2016 [25], corresponds to a function $d : X \times Y \to [0, \infty)$ that aims to model the mutual distance between the elements of two nonempty sets X and Y, such that the function satisfies the following properties:

(B1) $\forall (x, y) \in X \times Y$, if $d(x, y) = 0$ then $x = y$,
(B2) $\forall u \in X \cap Y$, $d(u, u) = 0$,
(B3) $\forall u, v \in X \cap Y$, $d(u, v) = d(v, u)$,
(B4) $\forall (x, y), (x', y') \in X \times Y$, $d(x, y) \leq d(x, y') + d(x', y') + d(x', y)$.

Since many real-life applications to be considered require the sets X and Y to be disjoint, that is, $X \cap Y = \emptyset$, (B2) and (B3) become completely irrelevant, and (B1) merely states that the function d must always take a positive value. Thus, the only axiom that is decisive for our purposes is (B4), known as the quadrilateral inequality, and the remainder of the study is built upon this inequality.

Every bipolar metric $d : X \times Y \to [0, \infty)$ induces a pseudo-metric on each of the sets X and Y, called inner pseudo-metrics [25]. These pseudo-metrics make it possible to define distances; hence, in a sense, similarity measures among elements of the same type.

2.1. Construction of the Model and Quadrilateral Inequality Compliance Indices.

Let $X = \{x_1, \ldots, x_m\}$ and $Y = \{y_1, \ldots, y_n\}$ be two disjoint finite sets, and consider a function $d : D \subseteq X \times Y \to (0, \infty)$. (Since the sets are assumed to be disjoint for the application, the value 0 is not included in the codomain of the function.)

The value $d(x, y)$ represents a "bipolar distance" defined via observed or processed data between $x \in X$ and $y \in Y$. We aim to measure the extent to which d complies with the quadrilateral inequality.

To test the quadrilateral inequality, we consider quadruples for which the four distances appearing in the inequality are defined. For this purpose, define

$$Q = \Big\{(x, x', y, y') \in X \times X \times Y \times Y : d(x, y),\ d(x, y'),\ d(x', y),\ d(x', y') \text{ are defined}\Big\}.$$

In the case of complete data, we have $|Q| = |X|^2|Y|^2$. If missing data are present, then $|Q| < |X|^2|Y|^2$.

First, for each quadruple, define a function

$$H(x, x', y, y') = \begin{cases} 1, & \text{if } d(x, y) \leq d(x, y') + d(x', y') + d(x', y), \\ 0, & \text{otherwise.} \end{cases}$$

This is the characteristic function corresponding to the subset

$$\{(x, x', y, y') \in Q : d(x, y) \leq d(x, y') + d(x', y') + d(x', y)\}.$$

Let us define the binary compliance ratio that measures the proportion of cases in which the transformed distance data satisfy the quadrilateral inequality:

$$R_{\text{hard}} = \frac{1}{|Q|} \sum_{(x,x',y,y') \in Q} H(x, x', y, y').$$

Clearly, $R_{\text{hard}} \in [0, 1]$, and the case $R_{\text{hard}} = 1$ means that the quadrilateral inequality holds exactly, and therefore (X, Y, d) is a bipolar metric space, if $D = X \times Y$. This index is a coarse measure that does not take into account the magnitude of violations and measures, in a sense, how close d is to being a bipolar metric.

As a more refined measure, we may define a score that assigns the value 1 to the quadruples for which the inequality holds, while also taking into account the severity of violation in the cases where the inequality fails. For each $(x, x', y, y') \in Q$, define

$$S(x, x', y, y') = \begin{cases} 1, & \text{if } d(x, y) \leq d(x, y') + d(x', y') + d(x', y), \\ \dfrac{d(x, y') + d(x', y') + d(x', y)}{d(x, y)}, & \text{otherwise.} \end{cases}$$

Since in the case of violation we have

$$d(x, y) > d(x, y') + d(x', y') + d(x', y),$$

we obtain

$$0 \ < \ \frac{d(x, y') + d(x', y') + d(x', y)}{d(x, y)} \ < \ 1,$$

which yields a ratio indicating how severely the inequality is violated. Thus, we may define the average soft compliance index as

$$R_{\text{soft}} \ = \ \frac{1}{|Q|} \sum_{(x,x',y,y') \in Q} S(x, x', y, y').$$

This index also lies in the interval $[0, 1]$, and the value 1 again means that d is a bipolar metric, if $D = X \times Y$. The quantity R_{soft} is a more sensitive compliance measure that summarizes the magnitude of violations in a single value, but it has a higher computational cost.

In every case, it is clear that $R_{\text{soft}} \geq R_{\text{hard}}$, and since all $d(x, y)$ values are nonzero, equality can only occur when both indices are equal to 1.

2.2. **Possible Lower and Upper Bounds for Missing Data.** Now suppose that some values of the function d are missing, or that we wish to enlarge the sets by adding new elements whose measurements have been only partially performed.

For example, let $a \in X$ and $b \in Y$ be such that $d(a, b)$ is unknown, while for many $(x, y) \in X \times Y$ the values $d(a, y)$, $d(x, b)$, and $d(x, y)$ are known. By using the quadrilateral inequality in a systematic manner, we may propose an upper and a lower bound for $d(a, b)$. To this end, define

$$Q_{ab} = \Big\{(x, y) \in X \times Y : d(x, y),\ d(a, y),\ d(x, b) \text{ are defined}\Big\}.$$

Since the quadrilateral inequality requires

$$d(a, b) \leq d(a, y) + d(x, y) + d(x, b)$$

to hold for every $(x, y) \in Q_{ab}$, the quantity

$$U(a, b) = \inf_{(x,y) \in Q_{ab}} \big(d(a, y) + d(x, y) + d(x, b)\big)$$

is a theoretical upper bound for $d(a, b)$. Intuitively, $U(a, b)$ may be interpreted as the cost of the cheapest indirect path between a and b.

To obtain a lower bound, we may rewrite the quadrilateral inequality with different choices and move the term $d(a, b)$ to the right-hand side. In this case, we may define

$$L(a, b) = \sup_{(x,y) \in Q_{ab}} \max\Big(d(x, y) - d(a, y) - d(x, b),\ d(a, y) - d(x, y) - d(x, b),\ d(x, b) - d(x, y) - d(a, y),\ 0\Big)$$

as a lower bound. Then, we expect the inequality

$$L(a, b) \leq d(a, b) \leq U(a, b)$$

to hold to the extent that the data comply with the quadrilateral inequality.

As will be seen in the example considered, these bounds may correspond to excessively wide intervals, and therefore their practical significance may remain limited.

2.3. **Approximate Imputation via the Quadrilateral Inequality Ratio.** For each $(x, x', y, y') \in Q$, define the quadrilateral inequality ratio by

$$R(x, x', y, y') = \frac{d(x, y)}{d(x, y') + d(x', y') + d(x', y)}.$$

Although for bipolar metric spaces we must have $R \leq 1$, and we may expect many data points that do not form a bipolar metric to nonetheless satisfy this inequality, it is still possible to encounter extreme cases with $R > 1$.

Since R is always positive by the assumption that $X \cap Y = \emptyset$, and, moreover, a multiplicative quantity, we may prefer to use the geometric mean. Based on the known data, we define a universal imputation coefficient by

$$M_{\text{geo}}(R) = \sqrt[|Q|]{\prod_{(x,x',y,y') \in Q} R(x, x', y, y')} = \exp\left(\frac{1}{|Q|} \sum_{(x,x',y,y') \in Q} \ln R(x, x', y, y')\right).$$

Now, suppose that $d(a, b)$ is unknown for some $a \in X$ and $b \in Y$. The coefficient $M_{\text{geo}}(R)$ represents the average multiplicative relaxation level of the quadrilateral inequality in the data, and it may be interpreted as summarizing the typical behavior

$$d(a, b) \approx M_{\text{geo}}(R)\,[d(x, b) + d(x, y) + d(a, y)].$$

Accordingly, using again a geometric-mean-based approach, we may estimate $d(a, b)$ by

$$\widehat{d}(a, b) = M_{\text{geo}}(R)\, \exp\left(\frac{1}{|Q_{ab}|} \sum_{(x,y) \in Q_{ab}} \ln(d(x, b) + d(x, y) + d(a, y))\right).$$

2.4. **Detecting the Closest Pairs Using Inner Pseudo-Metrics.** Given a bipolar metric on the sets X and Y, we also obtain the inner pseudo-metrics defined by

$$d_X(x_1, x_2) = \sup_{y \in Y} |d(x_1, y) - d(x_2, y)| \quad \text{and} \quad d_Y(y_1, y_2) = \sup_{x \in X} |d(x, y_1) - d(x, y_2)|,$$

as introduced in [25]. Since these expressions involve a supremum, they are theoretically quite strict, yet at the same time they provide extremely simple, practical, and meaningful measures for identifying similar pairs of the same type. Naturally, more flexible variants that are less sensitive to extreme values, such as versions based on some measure of central tendency instead of the supremum, can be easily formulated statistically. However, since this study focuses on the practical reflections of bipolar metric space theory, no such modification is made in this formulation.

3. Modeling Ligand–Target Interactions with a Bipolar Metric

In this section, we aim to test the bipolar metric space structure for the first time on a real measurement table. Among many potential application candidates, the interaction between ligands and the protein kinases they target has been chosen as an inaugural example. Kinases are enzymes that transmit critical intracellular signals and play roles in diseases such as cancer, Alzheimer's, and inflammation. Ligands, on the other hand, are small molecules with the potential to bind to proteins. Ligands are often intended as drug molecules, and understanding how strongly a ligand binds to a given protein is one of the fundamental questions in drug development, since strong binding may inhibit a kinase and thus be therapeutically beneficial.

In this study, a subset of the KIBA dataset [40], which contains interaction scores between protein kinase inhibitors and their biological targets, has been examined. This dataset presents a matrix of measurement scores describing the binding activities between ligands and protein kinase targets, where higher scores correspond to stronger binding. Here, only the numerical structure relevant to the mathematical framework has been used; a biochemical content analysis has not been intended. The data were obtained from a processed version available on Kaggle.[1]

The measurements in the database exhibit a heterogeneous distribution for both ligands and targets, meaning that some have many recorded measurements while others have few. In this work, we selected the 100 targets with the highest number of measurements and, for these targets, the 100 ligands with the highest number of cross-measurements, resulting in a 100×100 submatrix. This matrix contains 9873 entries, corresponding to a density of 98.73%.

[1] https://www.kaggle.com/datasets/rajaryan2315/davis-and-kiba-datasets/data

In the chosen submatrix, ligands are considered as the set X and targets as the set Y. Letting $s(x, y)$ denote the binding score corresponding to the ligand–target pair (x, y), the partial function $d : X \times Y \to \mathbb{R}_0^+$ was defined, for all pairs with known scores, by

$$d(x, y) = e^{-s(x,y)}.$$

This choice, one among many possible options, was made because stronger binding can naturally be interpreted as a measure of proximity, and because avoiding the value zero is desirable for our purposes.

The computations performed on the data show that, under this adjustment, the quadrilateral inequality is satisfied almost perfectly, with $R_{\text{hard}} \approx 0.9908$ and $R_{\text{soft}} \approx 0.9983$. The geometric mean of the quadrilateral inequality ratio used in the model was found to be $M_{\text{geo}}(R) \approx 0.302$.

To determine how the transformed distance matrix behaves under a missing-data scenario, a total of 1974 entries, corresponding to approximately 20% of the inputs, were removed.

The analysis revealed that approximately 62.8% of the true values satisfied the previously proposed bound $L(x, y) \leq d(x, y) \leq U(x, y)$. Accordingly, the deterministically derived bounds are neither excessively loose nor excessively tight; although many interval estimates fall short of perfection, they still offer a certain degree of meaningful safety margin.

When the values $\hat{d}(x, y)$ were computed for the missing entries, the mean absolute error relative to the true data was found to be around 2.99×10^{-6}, corresponding to approximately 61.9% mean relative error. However, this phenomenon is primarily a temporary exaggeration caused by the use of the exponential function in transforming scores to bipolar metric values, and much more reasonable imputation errors were obtained when score estimates were computed via the inverse transformation $\hat{s}(x, y) = -\ln \hat{d}(x, y)$.

The mean absolute error of the estimated scores compared to the true values was approximately 0.39, and the relative error was around 3.2%. These results show that the binding scores can be reconstructed with an error rate of nearly three percent, demonstrating that the method provides biologically meaningful accuracy in missing-data completion.

After testing the missing-data scenario, the values for the inner pseudo-metric d_X among ligands and d_Y among targets were also computed.

For example, in the selected subset, the two closest molecules according to the value $d_X \approx 3 \times 10^{-6}$ have the following SMILES strings:

CC(C)(CO)CNc1nccc(-c2c(-c3ccc(F)cc3)nc3cnccn23)n1

and

Cc1nccn2c(-c3ccnc(NCC4(O)CC4)n3)c(-c3ccc(F)cc3F)nc12.

Another example, with $d_X \approx 5 \times 10^{-6}$, corresponds to the SMILES strings

CCOc1nc(C(=O)NCc2ccc(S(C)(=O)=O)cc2)cc(N)c1Cl

and

CCOc1nc(NC(=O)Cc2cc(OC)c(S(C)(=O)=O)cc2OC)cc(N)c1C#N.

In general, closely related ligand pairs tend to share similar scaffolds and differ only by small functional group variations. On the other hand, d_X values can reach approximately 5×10^{-5}, and such pairs tend to possess different pharmacophores, charge distributions, and steric profiles.

A similar phenomenon is observed for the targets. For instance, the smallest d_Y value, about 5×10^{-6}, occurs between the pair of targets whose first 60 amino acids are

MASTTTCTRFTDEYQLFEELGKGAFSVVRRCMKIPTGQEYAAKIINTKKLSARDHQKLER...

and

MATTATCTRFTDDYQLFEELGKGAFSVVRRCVKKTSTQEYAAKIINTKKLSARDHQKLER...,

where it is notable that more than 90% of the first amino acids are identical, with only small substitutions at a few positions.

Finally, we apply the proposed model to predict 10 of the 127 ligand–target pairs in the 100×100 data matrix for which no experimental measurements were available or recorded in the database, and we present the predicted values in Table 1

Ligand (SMILES)	Target (AA sequence, first 60 aa)	Estimated Score
CC(=O)c1cccc(-c2cnc3[nH]ccc3c2)c1	MDRSKENCISGPVKATAPVGGPKRVLVTQQFPCQNPLPVNSGQAQRVPD...	11.7796
COc1cc(-c2ccc3c(c2)NC(=O)c2ccc(-c4ccccc4NS(C)(=O)=O)cc2)ccc3	MGCIKSKGKDSLSDDGVDLKTQPVRNTERTIYVRDPTSNKQQRPVPAS...	11.7766
CN1CCN(c2nc(C3=C(c4c[nH]c5ccccc45)C(=O)NC3=O)c3ccccc3n2)CC1	MSSARTPLPTLNERDTEQPTLGHLDSKPSSKSNMIRGRNSATSADED...	11.6991
NCCCn1cc(-c2cc(-c3cc4ccccc4s3)c3[nH]ncc3c2)c2nc3ccccc3n2	MRRRRRRDGFYPAPDFRDREAEDMAGVFDIDLDQPEDAGSEDELEEE...	11.8545
Nc1noc2cccc(-c3cccc(O)c3)c12	MNKPITPSTYVRCLNVGLIRKLSDFIDPQEGWKKLAVAIKKPSGDD...	11.4712
COCCOCC#Cc1cc(-c2n[nH]c3c2C(=O)c2cc(CN4CCN(C)CC4)c(F)cc2F)ccc3	MPALARDGGQLPLLVVFSAMIFGTITNQDLPVIKCVLINHKNNDSS...	11.8092
COC(C(=O)N1Cc2[nH]nc(NC(=O)c3ccc(N4CCN(C)CC4)c(F)cc3F)c2)N1	MGDPAPARSLDDIDLSALRDPAGIFELVEVVGNGTYGQVYKGRHVK...	11.7537
Nc1ccc(-c2cncc(OCC(N)Cc3c[nH]c4ccccc34)c2)cc1CN	MPHEPHEPLTPPFSALPDPAGAPSRRQSRQRPQLSSDSPSAFRASR...	11.5975
N#Cc1ccc2c(c1)C(=C1C=CC(CN3CCOCC3)=CN1)C(=O)N2	MLEICLKLVGCKSKKGLSSSSSCYLEEALQRPVASDFEPQGLSEAA...	11.8269
CCOc1nc(C(=O)NCc2ccc(S(C)(=O)=O)cc2)cc(N)c1C#N	MDVSLCPAKCSFWRIFLLGSVWLDYVGSVLACPANCVCSKTEINCR...	11.7899

TABLE 1. Theoretical KIBA score estimates for 10 ligand–target pairs with missing measurements.

4. CONCLUSION

In this study, the bipolar metric space structure was tested for the first time on a real dataset on the tenth anniversary of the theory. The scores in the dataset were transformed into possible bipolar metric values, the percentage of compliance with the quadrilateral inequality was measured, a missing-data imputation scenario was constructed, and results were obtained by examining the possible lower and upper bounds, estimated metric values, and within-group proximity measures. Consequently, some missing measurement values in the relevant dataset were also estimated. It was found that the ligand–target interaction score predictions were meaningfully accurate, with an approximate relative error of 3.2%. Thus, a model for applying bipolar metrics to real datasets has been demonstrated as a feasible approach, paving the way for similar studies to be tested across a wide variety of fields in the natural and social sciences.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this article.

AUTHORS CONTRIBUTION STATEMENT

Each author equally contributed to this paper.

REFERENCES

[1] Åqvist, J., Luzhkov, V.B., Brandsdal, B.O., *Ligand binding affinities from MD simulations*, Accounts of Chemical Research, **35**(6)(2002), 358–365.

[2] Atchley, W., Wingenbach, G., Akers, C., *Comparison of course completion and student performance through online and traditional courses*, International Review of Research in Open and Distributed Learning, **14**(4), 104–116. (2013)

[3] Batista-Foguet, J.M., Fortiana, J., Currie, C., Villalbí, J.R., *Socio-economic indexes in surveys for comparisons between countries*, Social Indicators Research, **67**(3)(2004), 315–332.

[4] Bell, R.P., *The rates of simple acid–base reactions*, Quarterly Reviews, Chemical Society, **13**(3)(1959), 169–182.

[5] Bhardwaj, R., *Existence and uniqueness of solutions of nonlinear integral equations through results in fuzzy bipolar metric spaces*, Journal of Nonlinear Modeling and Analysis, **7**(2025)(2), 399–413.

[6] Bhavani, C.U., Naresh, P., Rao, B.S., Reddy, G.U., *Innovative approaches to* (A, B)*-contraction and* T*-coupling fixed points in bipolar parametric metric spaces*, Adv. Fixed Point Theory, **15**(1)(2025), 16.

[7] Bretz, S.L., Linenberger, K.J., *Development of the enzyme–substrate interactions concept inventory*, Biochemistry and Molecular Biology Education, **40**(4)(2012), 229–233.

[8] Çetin, S., Gürdal, U., *Characterization of bipolar ultrametric spaces and fixed point theorems*, Hacettepe Journal of Mathematics and Statistics, **52**(1)(2023), 185–196.

[9] Copeland, R.A., *The dynamics of drug-target interactions: drug-target residence time and its impact on efficacy and safety*, Expert Opinion on Drug Discovery, **5**(4)(2010), 305–310.

[10] Costello, R., Toshkov, D., Bos, B., Krouwel, A., *Congruence between voters and parties: the role of party-level issue salience*, European Journal of Political Research, **60**(1)(2021), 92–113.

[11] Ghasab, E.L., De la Sen, M., *Solving damped harmonic oscillator as a second-order differential equations and Caputo fractional differential equation in bipolar Menger probabilistic b-metric spaces*, International Journal of Analysis and Applications, **23**(1)(2025), 133.

[12] Grant, P.R., *Ecological compatibility of bird species on islands*, The American Naturalist, **100**(914)(1966), 451–462.

[13] Gupta, V., Anju, A., Thakur, D., Sehgal, I., *Existence of fixed points in neutrosophic bipolar fuzzy metric spaces with application*, Journal of the Indonesian Mathematical Society, **31**(3)(2025), 1601.

[14] Gürdal, U., Mutlu, A., Özkan, K., *Fixed point results for* α*-*ψ*-contractive mappings in bipolar metric spaces*, J. Inequal. Spec. Funct., **11**(1)(2020), 64–75.

[15] Gürdal, U., Yapalı, R., Mutlu, A., *Generalized Kuratowski closure operators in the bipolar metric setting*, Proceedings of International Mathematical Sciences, **6**(1)(2024), 1–17.

[16] Hirschenhauser, K., Meichel, Y., Schmalzer, S., Beetz, A.M., *Children love their pets: do relationships between children and pets co-vary with taxonomic order, gender, and age?*, Anthrozoös, **30**(3)(2017), 441–456.

[17] Hussaina, N., Alharbib, N., Basendwaha, G., *Solving multi-order fractional differential equations using covariant contraction principle*, J. Math. Computer Sci., **39**(1)(2025), 71–89.

[18] Jeevanandam, U.M., Kathavarayan, D., Raveendran, S.B., Azmi, F., Mlaiki, N., *Fixed point theorems on $\aleph$-extended fuzzy bipolar b-metric spaces*, International Journal of Analysis and Applications, **22**(1)(2024), 223–223.

[19] Kishore, G.N.V., Rao, B.S., Prasad, D.R., Radenović, S., *Multivalued Δ-symmetric covariant results in bipolar metric spaces*, Zhurnal Sibirskogo federal'nogo universiteta. Matematika i fizika, **17**(5)(2024), 575–585.

[20] Konwar, N., Debnath, P., *Fixed-point results of F-contractions in bipolar p-metric spaces*, Axioms, **13**(11)(2024), 773–773.

[21] Limprayoon, J., Bunpatcharacharoen, P., Mungkala, C., *Common interpolative rational type contractions in bipolar metric spaces*, Bangmod International Journal of Mathematical and Computational Science, **11**(1)(2025), 305–327.

[22] Mani, G., Ramaswamy, R., Gnanaprakasam, A.J., Elsonbaty, A., Abdelnaby, O.A.A., Radenović, S., *Application of fixed points in bipolar controlled metric space to solve fractional differential equation*, Fractal and Fractional, **7**(3)(2023), 242–242.

[23] Mebarki, K., Boudaoui, A., Belhenniche, A., Bota, M.F., *Fixed-point theorems for covariant and contravariant multivalued mappings in bipolar b-metric spaces*, Mathematics, **13**(18)(2025), 2983–2983.

[24] Murthy, P.P., Dhuri, C.P., Patel, U.D., *Common fixed point for w-compatible maps in a bipolar metric space*, Facta Universitatis, Series: Mathematics and Informatics, **1**(1)(2025), 421–438.

[25] Mutlu, A., Gürdal, U., *Bipolar metric spaces and some fixed point theorems*, Journal of Nonlinear Science and Applications, **9**(9)(2016), 1–1.

[26] Mutlu, A., Özkan, K., Gürdal, U., *Fixed point theorems for multivalued mappings on bipolar metric spaces*, Fixed Point Theory, **21**(1)(2020), 271–280.

[27] Mutlu, A., Özkan, K., Gürdal, U., *Locally and weakly contractive principle in bipolar metric spaces*, TWMS Journal of Applied and Engineering Mathematics, **10**(2)(2020), 379–388.

[28] Neri, D., Montigiani, S., Kirkham, P.M., *Biophysical methods for the determination of antibody-antigen affinities*, Trends in Biotechnology, **14**(12)(1996), 465–470.

[29] Olaleru, J.O., Apanpa, K.I., Mogbademu, A.A., *Fixed point results of Hardy and Rogers mappings in bipolar metric spaces with application to integral equations*, Open Journal of Mathematical Sciences (OMS), **9**(1)(2025), 233–244.

[30] Özkan, K., Gürdal, U., Mutlu, A., *Caristi's and Downing-Kirk's fixed point theorems on bipolar metric spaces*, Fixed Point Theory, **22**(2)(2021), 785–785.

[31] Rajitha, V., Reddy, G.U., *On some quadruple fixed points of covariant mappings in bipolar metric spaces with applications*, Adv. Fixed Point Theory, **14**(1)(2024), 34.

[32] Ramaswamy, R., *Fixed point theorems on multiplicative cone bipolar metric space and their applications*, European Journal of Pure and Applied Mathematics, **18**(4)(2025), 1.

[33] Rani, J., Prakasam, A., *Fixed points of operators with multiplicative closed graphs on bipolar b-multiplicative metric spaces*, Adv. Fixed Point Theory, **14**(1)(2024), 57.

[34] Rao, S., Tarani, K.C.N., Murthy, N.V.E.S., Srinuvasa Rao, B., *Certain applications of JS-quasi-contraction fixed point theorems in bipolar metric spaces*, Adv. Fixed Point Theory, **14**(1)(2024), 31.

[35] Sarwar, M., Ali, N., Abodayeh, K., Promsakon, C., Sitthiwirattham, T., *Contravariant Reich type F-contraction in F-bipolar metric spaces with application*, Results in Nonlinear Analysis, **8**(2)(2025), 328–336.

[36] Schumaker, B.L., *Apparent brightness of stars and lasers*, TDA Progress Report, 1988, 42–93.

[37] Sedghi, S., Sımkha, M., Gürdal, U., Mutlu, A., *Fixed point theorems for contravariant maps in bipolar b-metric spaces with integration application*, Proceedings of International Mathematical Sciences, **6**(1)(2024), 29–43.

[38] Stanford, G., DeMent, J.D., *A method for measuring short-term nutrient absorption by plants: I. Phosphorus*, Soil Science Society of America Journal, **21**(6)(1957), 612–617.

[39] Taleb, M.M., Borkar, V.C., *Fixed point theorems in triple-composed bipolar metric spaces and its application to solving coupled ordinary differential equations*, Palestine Journal of Mathematics, **14**(1)(2025), 1.

[40] Tang, J., Szwajda, A., Shakyawar, S., Xu, T., Hintsanen, P., Wennerberg, K., Aittokallio, T., *Making sense of large-scale kinase inhibitor bioactivity data sets: a comparative and integrative analysis*, Journal of Chemical Information and Modeling, **54**(3)(2014), 735–743.

[41] Varalakshmi, K., Reddy, G.U., *On some applications of P-contraction fixed point theorems in bipolar metric spaces*, International Journal of Analysis and Applications, **22**(1)(2024), 159.

[42] Wang, A., Zhang, Q., Shuangyao, Z., Xiaonong, L., Zhanglin, P., *A review-driven customer preference measurement model for product improvement: sentiment-based importance–performance analysis*, Information Systems and eBusiness Management, **18**(1)(2020), 61–88.

[43] Wong, K.S., Salleh, Z., Akhadkulov, H., Kuljanov, U.N., *Exploring Proinov-type and Banach-type contractions in fuzzy bipolar metric spaces*, Journal of Inequalities and Applications, **2025**(1)(2025), 94.

[44] Yadav, S., Ughade, M., Shukla, M.K., *Fixed-points of interpolative Kannan type contractions in bipolar metric spaces*, Adv. Fixed Point Theory, **13**(1)(2023), 24.

[45] Younis, M., Mutlu, A., Ahmad, H., *Ćirić contraction with graphical structure of bipolar metric spaces and related fixed point theorems*, Hacettepe Journal of Mathematics and Statistics, **1**(1)(2024), 1–19.