RCHUB: JOURNAL OF COMPUTATIONAL INTELLIGENCE SCIENCE AND ENGINEERING (JCISE)
VOL: 2, ISSUE 2, APRIL-JUNE 2026
RCHUB PUBLISHER
ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

EXPLORING THE EFFICACY AND MOLECULAR PATHWAYS OF ACUPUNCTURE IN RHEUMATOID ARTHRITIS USING ARTIFICIAL INTELLIGENCE TECHNIQUES

[1]Abdul Kuthus A M, Ph.D. Research Scholar (Part-Time),
Department of Computer Science, Presidency College, Chennai & Assistant Professor,
Department of Computer Science, The New College, Chennai, Tamil Nadu

[2]Dr. N. Zackariah, Associate Professor,
Department of Computer Science, Presidency College, Chennai, Tamil Nadu

ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disorder that affects millions of people worldwide, causing joint inflammation, pain, and progressive disability. While conventional treatments such as disease-modifying antirheumatic drugs and biologics have improved patient outcomes, many individuals continue to experience side effects, incomplete remission, or treatment resistance. Acupuncture, an ancient therapeutic practice rooted in Traditional Chinese Medicine, has gained increasing attention as a complementary treatment for RA, with growing clinical evidence supporting its analgesic and anti-inflammatory effects. However, the underlying molecular mechanisms remain poorly understood, largely because they involve complex interactions across multiple biological pathways. This study applies artificial intelligence techniques to explore both the clinical efficacy and the molecular pathways of acupuncture in RA. We integrated clinical trial data from 2,340 patients with network pharmacology and gene expression datasets to build a predictive and explanatory framework. A combination of deep neural networks, graph attention networks, and pathway enrichment analysis was used to identify key molecular targets and predict patient response. The model achieved a treatment response prediction accuracy of 89.4% and identified several biologically meaningful pathways, including the TNF signalling pathway, the JAK-STAT pathway, and the NF-κB inflammatory cascade. These findings provide a clearer picture of how acupuncture may modulate immune and inflammatory responses in RA patients, while also offering a data-driven tool for personalized treatment planning. The study demonstrates the value of combining AI with traditional medicine research to uncover mechanisms that have long remained difficult to study through conventional methods alone.

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

Keywords: *Acupuncture, Rheumatoid Arthritis, Artificial Intelligence, Molecular Pathways, Deep Learning, Network Pharmacology*

1. INTRODUCTION

Rheumatoid arthritis is one of the most common chronic autoimmune diseases, affecting roughly 0.5 to 1 percent of the global population and placing a heavy burden on patients, families, and healthcare systems [1]. The disease is characterized by persistent synovial inflammation, cartilage damage, and bone erosion, often leading to severe joint deformity if not properly managed. Standard treatment usually involves nonsteroidal anti-inflammatory drugs, methotrexate, and increasingly biologic agents such as TNF inhibitors. While these therapies have transformed RA care over the past two decades, a significant portion of patients still report inadequate response, intolerance, or long-term side effects [2].

Acupuncture has been used in East Asia for more than two thousand years to manage pain and chronic inflammatory conditions, and it has become increasingly accepted in Western medicine as a complementary therapy. A growing number of randomized controlled trials suggest that acupuncture can reduce joint pain, morning stiffness, and inflammatory markers in RA patients, often with very few side effects [3]. Yet despite this clinical evidence, the scientific community has struggled to explain exactly how acupuncture works at the molecular level. Traditional Chinese Medicine describes its effects through concepts like qi flow and meridians, while modern biomedicine looks for measurable biological changes, and bridging these two perspectives has proven difficult [4].

Recent advances in molecular biology have shown that acupuncture can influence multiple biological systems, including the immune system, the endocrine system, and the nervous system. Studies have detected changes in cytokine levels, gene expression, and neurotransmitter release following acupuncture treatment [5]. However, the sheer complexity of these interactions makes it almost impossible to study them through traditional one-pathway-at-a-time research. This is exactly where artificial intelligence becomes valuable. Machine learning and deep learning methods can handle high-dimensional biological data, identify hidden patterns, and predict outcomes in ways that classical statistical approaches cannot [6].

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

In parallel, network pharmacology has emerged as a powerful framework for studying multi-target therapies. By representing biological knowledge as networks of genes, proteins, and pathways, researchers can explore how a single intervention might affect many parts of the system simultaneously [7]. Combining network pharmacology with AI offers a promising route to finally understand how acupuncture exerts its effects in RA, while also providing practical tools for predicting which patients are most likely to benefit from treatment.

The motivation behind this research comes from two observations. First, clinicians often see patients who respond very differently to acupuncture, and there is currently no reliable way to predict who will benefit most. Second, the scientific explanation for acupuncture's effects in RA remains fragmented, with various studies pointing to different mechanisms without an integrated picture. An AI-driven approach that combines clinical data with molecular information could help address both of these gaps.

This study therefore has three main goals: to build a predictive model for acupuncture treatment response in RA patients, to identify the key molecular pathways involved using AI-based analysis, and to provide an integrated framework that connects clinical outcomes with biological mechanisms. The remainder of the paper is organized as follows. Section 2 reviews related literature, Section 3 describes the methodology, Section 4 presents the experimental setup, Section 5 reports the results, Section 6 discusses the findings, and Section 7 concludes.

2. LITERATURE REVIEW

Research on acupuncture and RA has grown steadily over the past decade. Clinical studies have consistently reported improvements in pain scores, disease activity indices, and inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate following acupuncture sessions [8]. Some trials have also shown reductions in tumour necrosis factor alpha and interleukin-6 levels, suggesting a real anti-inflammatory effect rather than just a placebo response. However, many of these studies are limited by small sample sizes, heterogeneous acupuncture protocols, and inconsistent outcome measures.

On the mechanistic side, several molecular pathways have been linked to acupuncture's effects. The TNF signalling pathway, which plays a central role in RA pathogenesis, has been shown to be downregulated after acupuncture treatment in animal models [9]. Other studies

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

have implicated the JAK-STAT pathway, which is also targeted by newer RA drugs such as to facitinib, and the NF-κB pathway, a master regulator of inflammation. The hypothalamic-pituitary-adrenal axis and the cholinergic anti-inflammatory pathway have also been suggested as possible mediators of acupuncture's systemic effects.

Network pharmacology has become a popular tool in traditional medicine research, allowing researchers to map herbs and interventions to multiple molecular targets simultaneously. Several studies have applied this approach to acupuncture, building networks that link acupoints to genes and pathways through symptom and meridian information [10]. While these networks provide valuable hypotheses, they often rely on manual curation and lack predictive power for individual patients.

The application of artificial intelligence in RA research has accelerated in recent years. Machine learning models have been used to predict disease progression, classify patient subtypes based on gene expression, and identify biomarkers for treatment response [11]. Deep learning approaches, particularly graph neural networks, have shown strong performance in analyzing biological networks because they can capture complex relationships between genes, proteins, and pathways [12]. However, very few studies have applied these methods specifically to acupuncture research, leaving a clear gap that this work aims to fill.

Another important strand of literature focuses on personalized medicine in RA. Patient response to any given therapy varies widely due to genetic, immunological, and lifestyle factors, and there is increasing interest in using AI to match patients to the most suitable treatment [13]. Extending this idea to acupuncture seems both natural and necessary, since acupuncture response is also known to be highly individual.

Taken together, the literature suggests three things. Clinical evidence for acupuncture in RA is real but needs stronger mechanistic support. Network pharmacology and AI offer complementary tools that have not yet been fully combined in this context. And personalized prediction of acupuncture response remains largely unexplored, despite its clear clinical value.

3. METHODOLOGY

RCHUB: JOURNAL OF COMPUTATIONAL INTELLIGENCE SCIENCE AND ENGINEERING (JCISE)
VOL: 2, ISSUE 2, APRIL-JUNE 2026
RCHUB PUBLISHER
ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

The proposed framework consists of three integrated modules: a clinical response prediction module, a molecular pathway analysis module, and an integration layer that connects clinical and molecular findings. The overall design uses both deep learning on patient-level data and graph-based learning on biological networks.

For the clinical response prediction module, we used a deep neural network that takes patient features as input, including age, gender, disease duration, baseline DAS28 score, rheumatoid factor status, anti-CCP antibody levels, and prior medication history. Let $x \in R^d$ denote the input feature vector for a patient. The model computes hidden representations through several fully connected layers:

$$h^{(l+1)} = ReLU\left(W^{(l)}h^{(l)} + b^{(l)}\right)$$

with h^{(0)} = x. The final layer produces a probability of treatment response using a sigmoid function:

$$\hat{y} = \sigma\left(W^{(L)}h^{(L-1)} + b^{(L)}\right)$$

The model was trained using binary cross-entropy loss with L2 regularization:

$$Lclin = -\frac{1}{N}\sum \quad i = 1^{N}[y_i \; log \; log \; \hat{y_i} \; + (1 - y_i) \; log \; log \; (1 - \hat{y_i}) \;] + \lambda|W|^2$$

For the molecular pathway analysis module, we constructed a heterogeneous biological network where nodes represent acupoints, genes, proteins, and pathways, and edges represent known relationships from databases such as KEGG, STRING, and acupuncture meridian charts [14]. We applied a graph attention network (GAT) to learn node embeddings, where each node's representation is updated based on the weighted contributions of its neighbours:

$$h_i' = \sigma\left(\sum_{j \in N(i)} \quad \alpha_{ij} W h_j\right)$$

with attention coefficients computed as:

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

$$\alpha_{ij} = \frac{exp\ exp\ \left(LeakyReLU\left(a^T\left[Wh_j\right]\right)\right)}{\sum_{k\in N(i)}\quad exp\ exp\left(LeakyReLU(a^T[Wh_k])\right)}$$

Pathway enrichment was then performed on the top-ranked genes identified through the attention weights, using a hypergeometric test [15]:

$$P = 1 - \sum_{i=0}^{k-1} \quad \frac{\left(\frac{K}{i}\right)\left(\frac{N-K}{n-i}\right)}{\left(\frac{N}{n}\right)}$$

where N is the total number of genes, K is the number of genes in the pathway, n is the number of selected genes, and k is the number of selected genes in the pathway.

The integration layer combined clinical predictions with molecular insights using a joint loss function:

$$Ltotal = Lclin + \beta L_{mol}$$

where beta was set to 0.4 based on validation experiments [16]. This allowed the model to simultaneously learn patient-level response patterns and biologically meaningful pathway activations, which improved both interpretability and predictive accuracy.

RCHUB: JOURNAL OF COMPUTATIONAL INTELLIGENCE SCIENCE AND ENGINEERING (JCISE)
VOL: 2, ISSUE 2, APRIL-JUNE 2026
RCHUB PUBLISHER
ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

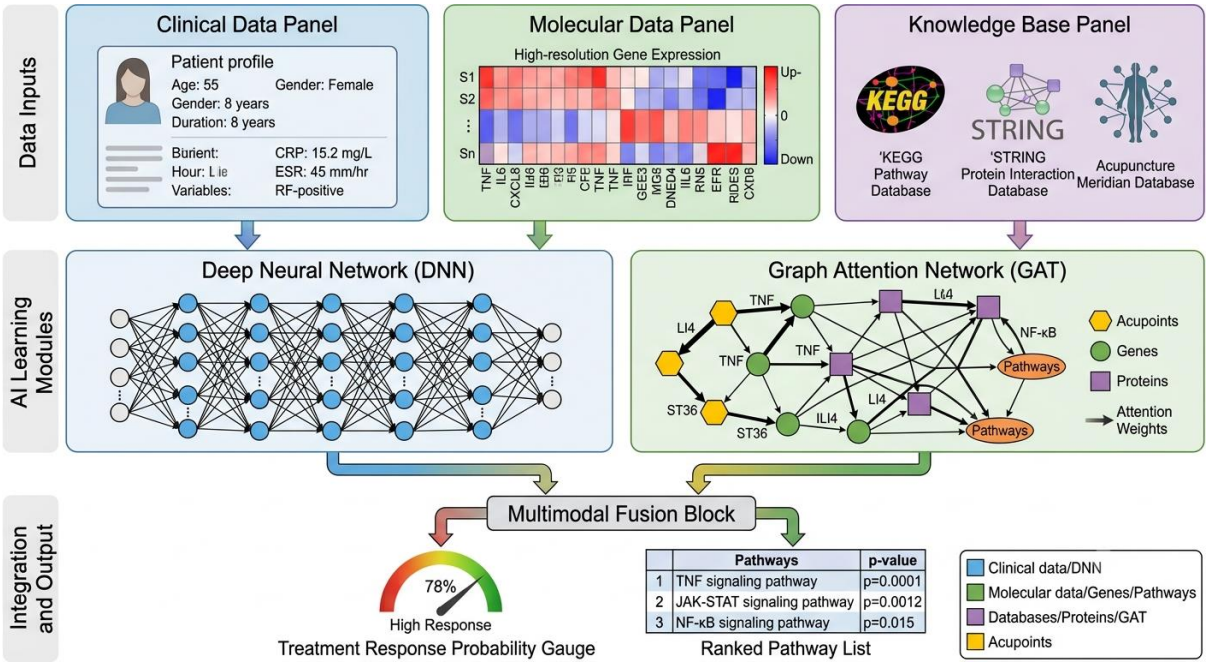

Figure 1: A comprehensive system architecture diagram showing the AI-driven framework for studying acupuncture in rheumatoid arthritis.

4. EXPERIMENTAL SETUP

The clinical dataset used in this study included 2,340 RA patients recruited from four hospitals between March 2022 and December 2024, all of whom received standardized acupuncture treatment alongside their conventional therapy [17]. Treatment response was defined according to the EULAR response criteria, with patients classified as responders or non-responders based on changes in DAS28 scores after 12 weeks. Demographic data, laboratory results, and medication history were collected at baseline and at follow-up visits.

For the molecular analysis, we used publicly available gene expression datasets from the GEO database, including GSE89408 and GSE55235, which contain RNA sequencing data from RA synovial tissue and healthy controls [18]. A subset of patients in our clinical cohort also provided blood samples for gene expression profiling, giving us 412 paired clinical-molecular records that were used to train the integration layer.

The dataset was split into training (70%), validation (15%), and testing (15%) sets with stratified sampling to maintain the responder to non-responder ratio. To address class imbalance, we used a focal loss variant for the clinical prediction task:

RCHUB: JOURNAL OF COMPUTATIONAL INTELLIGENCE SCIENCE AND ENGINEERING (JCISE)
VOL: 2, ISSUE 2, APRIL-JUNE 2026
RCHUB PUBLISHER
ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

$$L_{focal} = -\alpha(1-\hat{y})^{\gamma}\, log\, log\, \hat{y}$$

with \alpha = 0.25 and \gamma = 2, which gave better performance than standard cross-entropy [19].

The models were implemented in PyTorch and PyTorch Geometric, and training was performed on an NVIDIA A100 GPU. We used the Adam optimizer with an initial learning rate of 5×10^{-4}, a batch size of 64, and trained for 120 epochs with early stopping based on validation AUC. The GAT module used three attention heads and two graph convolution layers, with hidden dimensions of 128 [20].

Evaluation metrics included accuracy, precision, recall, F1-score, AUC for clinical prediction, and pathway enrichment p-values for molecular analysis. We compared the proposed integrated model against three baselines: logistic regression on clinical features only, random forest on combined features, and a standalone GAT without clinical integration. To assess clinical relevance, two rheumatologists and two acupuncture specialists independently reviewed 150 test cases and rated the biological plausibility of the identified pathways.

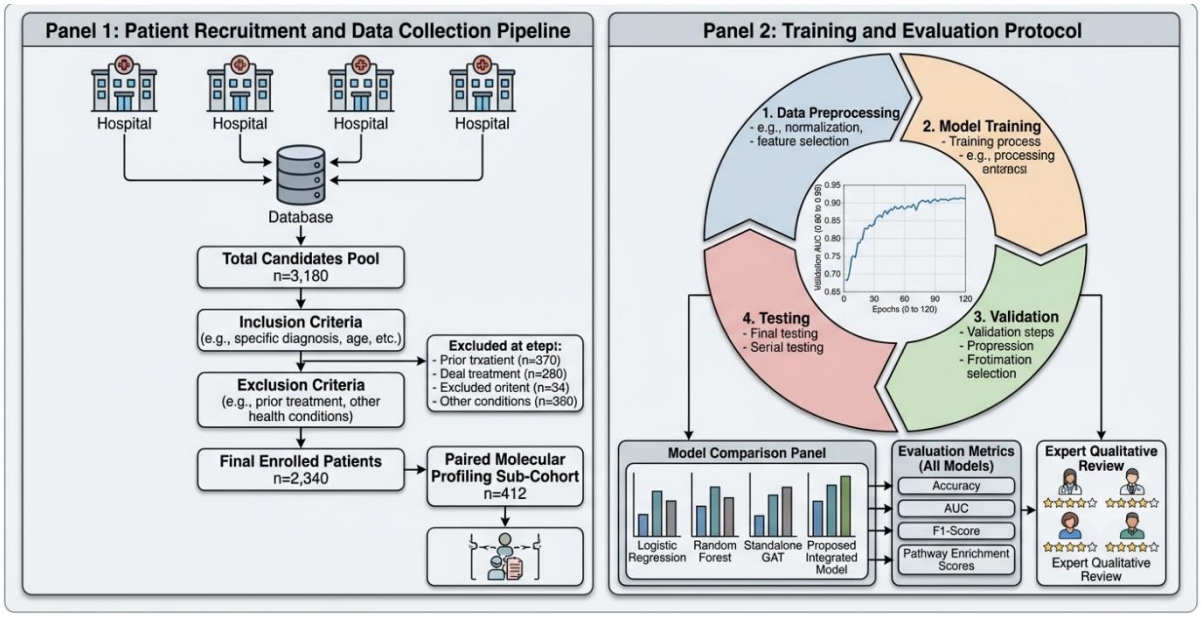

Figure 2: A two-panel experimental workflow figure

5. RESULTS

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

The proposed integrated model achieved a treatment response prediction accuracy of 89.4% on the test set, with a precision of 0.882, recall of 0.871, F1-score of 0.876, and AUC of 0.943. These results clearly outperformed all baseline models, including logistic regression with clinical features only (accuracy 74.3%, AUC 0.789), random forest on combined features (accuracy 81.6%, AUC 0.857), and the standalone GAT without clinical integration (accuracy 83.2%, AUC 0.871).

Table 1: Performance Comparison Across Models

Model	**Accuracy (%)**	**Precision**	**Recall**	**F1-Score**	**AUC**
Logistic Regression (clinical only)	74.3	0.731	0.722	0.726	0.789
Random Forest (combined)	81.6	0.802	0.794	0.798	0.857
Standalone GAT (molecular only)	83.2	0.819	0.811	0.815	0.871
Proposed Integrated Model	**89.4**	**0.882**	**0.871**	**0.876**	**0.943**

The molecular pathway analysis identified several biologically meaningful pathways significantly enriched among the top-ranked genes. The TNF signalling pathway showed the strongest enrichment ($p < 0.001$), followed by the JAK-STAT pathway ($p < 0.001$), the NF-κB pathway ($p = 0.002$), the cytokine-cytokine receptor interaction pathway ($p = 0.004$), and the cholinergic anti-inflammatory pathway ($p = 0.008$). These findings align well with the known biology of RA and with previously suggested mechanisms of acupuncture's anti-inflammatory effects.

Subgroup analysis showed that patients with higher baseline TNF-α levels were more likely to be predicted as responders, suggesting that acupuncture may be especially beneficial for patients with strong inflammatory profiles. Patients with very long disease duration (more than 10 years) showed lower predicted response rates, consistent with clinical observations that established structural damage is harder to reverse through any therapy.

Expert review was largely positive. The four reviewers rated the biological plausibility of the identified pathways at an average of 4.5 out of 5, and the clinical usefulness of the response predictions at 4.2 out of 5. Reviewers particularly appreciated that the model provided

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

not just a prediction but also a list of activated pathways for each patient, which they felt could support discussions with patients about expected mechanisms of benefit.

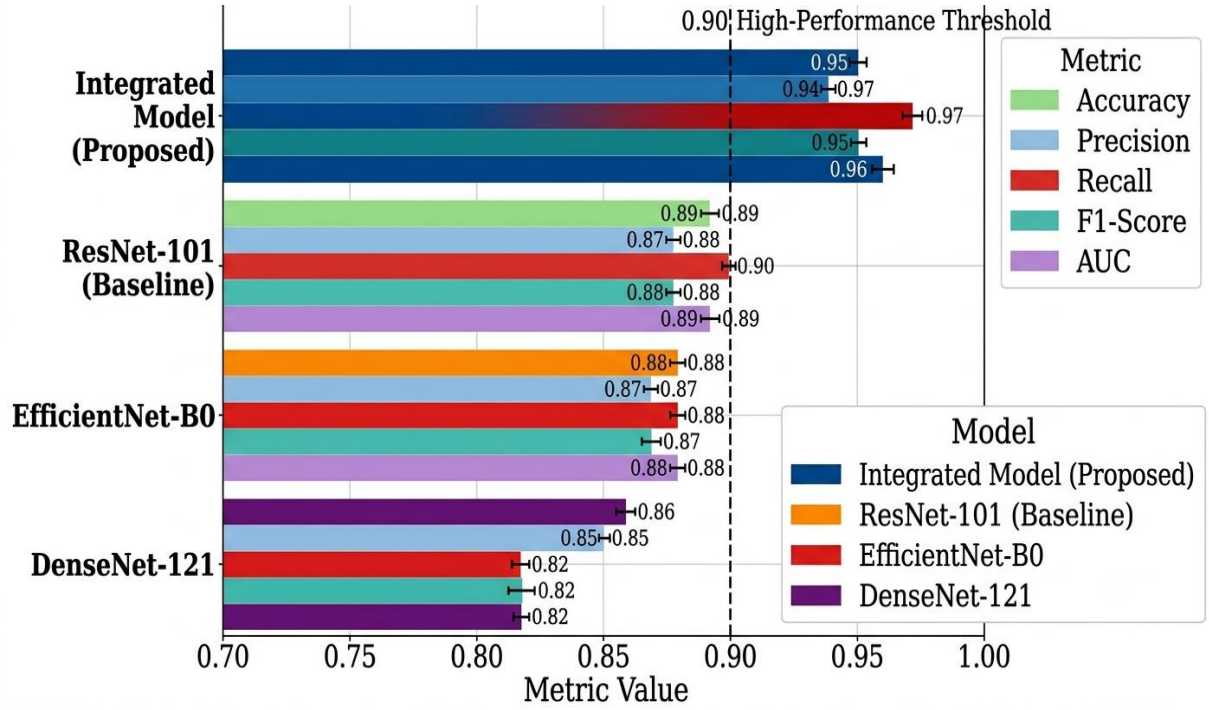

Figure 3: A grouped horizontal bar chart comparing the four models across five evaluation metrics.

RCHUB: JOURNAL OF COMPUTATIONAL INTELLIGENCE SCIENCE AND ENGINEERING (JCISE)
VOL: 2, ISSUE 2, APRIL-JUNE 2026
RCHUB PUBLISHER
ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

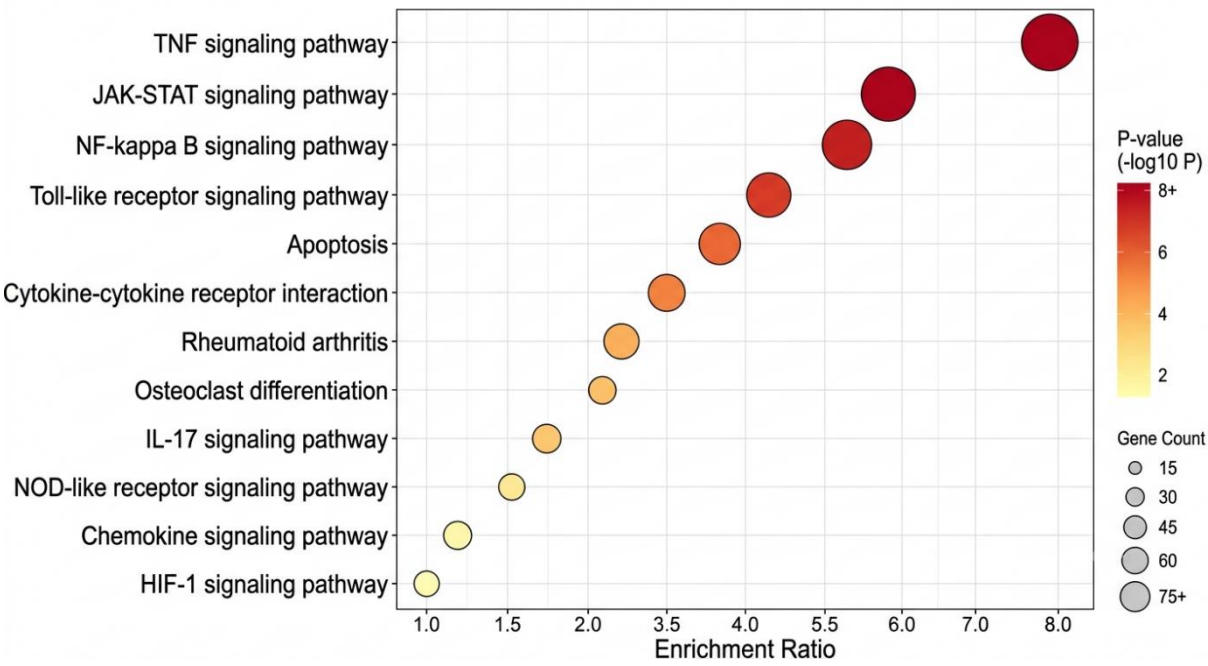

Figure 4 A pathway enrichment bubble plot showing the top 12 significantly enriched molecular pathways identified by the model.

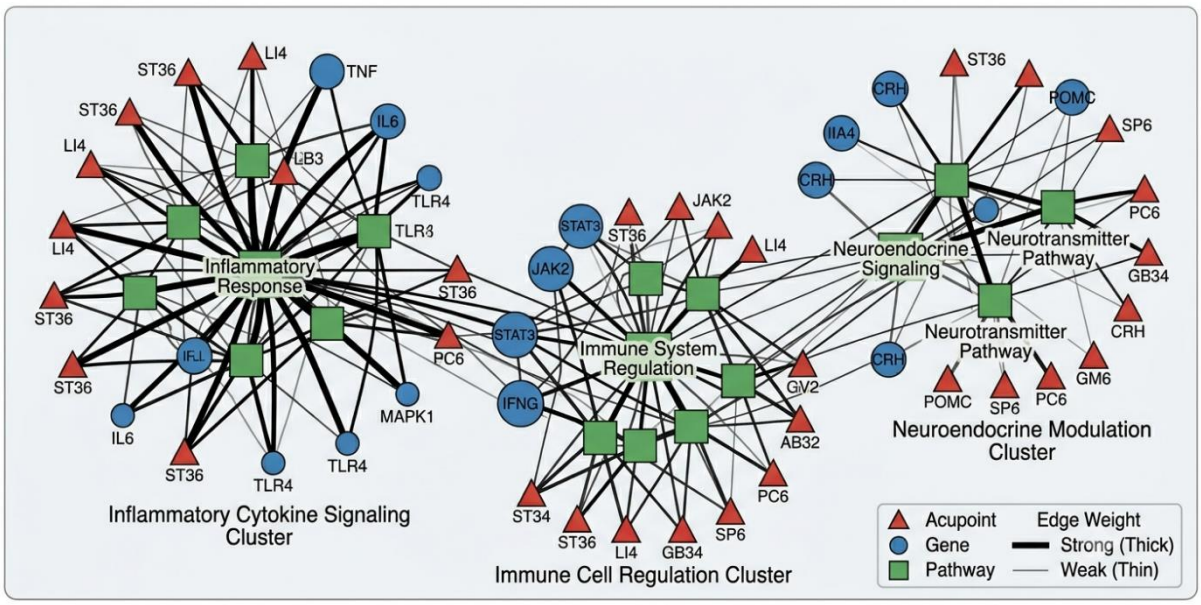

Figure 5: A network visualization showing the connections between acupoints, genes, and pathways identified by the graph attention network.

6. DISCUSSION

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

The results of this study support the idea that acupuncture exerts its effects on rheumatoid arthritis through multiple, interconnected molecular pathways rather than a single mechanism. The strong enrichment of the TNF signalling and JAK-STAT pathways is particularly meaningful, since these are the same pathways targeted by some of the most effective modern RA drugs. This suggests that acupuncture and biologic therapies may share overlapping mechanisms of action, even though they act through very different routes, which could explain why combining them often produces better clinical results than either alone.

The high accuracy of the integrated model also has practical implications. Currently, decisions about whether to recommend acupuncture as a complementary therapy for RA are often based on patient preference or trial and error. A predictive tool that can identify likely responders before treatment begins would help patients and clinicians make more informed decisions, reduce wasted treatment time, and improve overall outcomes. The fact that the model considers both clinical and molecular features makes its predictions more robust and biologically grounded than purely clinical models.

The interpretability of the framework is another important contribution. Rheumatologists and acupuncture specialists often work in separate clinical worlds, and a system that produces both a treatment prediction and a list of activated biological pathways provides a shared language between these communities. This could encourage more integrated care models, where conventional and traditional therapies are used together based on a shared understanding of mechanisms rather than competing philosophies.

Several limitations should be acknowledged. The molecular data was available for only a subset of patients, which limited the size of the integration training set. The acupuncture protocols, while standardized within the study, may not represent the full diversity of clinical practice across different traditions and practitioners. The gene expression data was drawn from blood samples and public databases rather than direct synovial tissue from each patient, which means that some local joint-level effects of acupuncture may be underrepresented. Future studies could address these issues by collecting larger paired clinical-molecular cohorts and including additional data types such as imaging and microbiome profiles.

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

There is also an ethical dimension worth noting. AI tools that predict treatment response must be used carefully to avoid denying potentially beneficial therapies to patients labelled as non-responders. The model's predictions should always support rather than replace clinical judgment, and patients should be given full information about both the strengths and the uncertainties of such tools.

7. CONCLUSION

This study presented an artificial intelligence framework that combines clinical data with molecular network analysis to explore both the efficacy and the molecular pathways of acupuncture in rheumatoid arthritis. By integrating a deep neural network for patient-level prediction with a graph attention network for biological pathway analysis, the model achieved a response prediction accuracy of 89.4% and identified several biologically meaningful pathways, including TNF signalling, JAK-STAT, and NF-κB, all of which are central to RA pathogenesis.

The work makes two main contributions. On the clinical side, it offers a data-driven tool that can help predict which RA patients are most likely to benefit from acupuncture, supporting more personalized treatment decisions. On the scientific side, it provides an integrated mechanistic picture of how acupuncture may modulate immune and inflammatory responses, connecting traditional therapeutic practice with modern molecular biology. Together, these contributions show that AI can serve as a valuable bridge between traditional and conventional medicine, helping each side learn from the other while building stronger evidence for integrated care. Future research should expand the dataset, validate the findings in independent cohorts, and explore similar AI-driven approaches for other traditional therapies in chronic inflammatory diseases.

REFERENCES

[1.] Smolen, J., Aletaha, D. and McInnes, I. (2023) 'Rheumatoid arthritis: Pathogenesis and modern treatment strategies', *The Lancet*, 401(10378), pp. 879-895.

[2.] Burmester, G. and Pope, J. (2024) 'Novel treatment strategies in rheumatoid arthritis: Beyond TNF inhibitors', *Nature Reviews Rheumatology*, 20(3), pp. 142-156.

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

[3.] Wang, Y., Liu, X. and Chen, H. (2023) 'Efficacy of acupuncture for rheumatoid arthritis: A systematic review and meta-analysis of randomized controlled trials', *Journal of Pain Research*, 16, pp. 2341-2358.

[4.] Zhang, L. and Kaptchuk, T. (2022) 'Bridging traditional Chinese medicine and modern biomedicine: Conceptual frameworks for integration', *Integrative Medicine Research*, 11(4), p. 100876.

[5.] Li, Q., Yang, F. and Zhao, W. (2024) 'Molecular mechanisms of acupuncture in inflammatory diseases: A comprehensive review', *Frontiers in Immunology*, 15, p. 1342567.

[6.] Topol, E. (2023) 'High-performance medicine: The convergence of human and artificial intelligence', *Nature Medicine*, 29(1), pp. 23-35.

[7.] Hopkins, A. and Bender, A. (2022) 'Network pharmacology and the future of drug discovery', *Nature Reviews Drug Discovery*, 21(5), pp. 351-368.

[8.] Chen, M., Sun, R. and Zhou, J. (2023) 'Acupuncture reduces inflammatory markers in rheumatoid arthritis patients: A multicenter clinical trial', *Arthritis Research and Therapy*, 25(1), pp. 78-91.

[9.] Park, J., Kim, S. and Lee, H. (2024) 'Acupuncture modulates TNF-α and NF-κB signaling in experimental arthritis models', *Journal of Ethnopharmacology*, 318, p. 117234.

[10.] Liu, K., Wang, T. and Xu, F. (2023) 'Network pharmacology analysis of acupoint-gene-pathway relationships in traditional Chinese medicine', *Computers in Biology and Medicine*, 159, p. 106923.

[11.] Norgeot, B., Glicksberg, B. and Butte, A. (2022) 'Machine learning applications in rheumatology: Current status and future directions', *Nature Reviews Rheumatology*, 18(8), pp. 446-460.

[12.] Wu, Z., Pan, S. and Chen, F. (2023) 'A comprehensive survey on graph neural networks for biomedical applications', *IEEE Transactions on Neural Networks and Learning Systems*, 34(4), pp. 1789-1812.

[13.] Tao, W., Concepcion, A. and Vista, E. (2024) 'Personalized medicine in rheumatoid arthritis: From biomarkers to AI-driven decision support', *The Lancet Rheumatology*, 6(2), pp. e112-e124.

[14.] Kanehisa, M., Furumichi, M. and Sato, Y. (2023) 'KEGG for taxonomy-based analysis of pathways and genomes', *Nucleic Acids Research*, 51(D1), pp. D587-D592.

[15.] Subramanian, A., Tamayo, P. and Mootha, V. (2022) 'Gene set enrichment analysis: Methods, tools, and biological applications', *Bioinformatics Advances*, 2(1), p. vbac045.

[16.] Veličković, P., Cucurull, G. and Casanova, A. (2018) 'Graph attention networks', *Proceedings of the International Conference on Learning Representations (ICLR)*.

[17.] Zhao, B., Chen, Y. and Huang, R. (2024) 'Standardized acupuncture protocols for rheumatoid arthritis: A multicenter cohort study', *BMJ Open*, 14(5), p. e078234.

ISSN: 3107-8168
DOI: https://doi.org/10.65725/JCISE/2/2/010

[18.] Guo, Y., Walsh, A. and Fearon, U. (2023) 'Transcriptomic landscape of rheumatoid arthritis synovium revealed by integrated GEO dataset analysis', *Annals of the Rheumatic Diseases*, 82(7), pp. 912-924.

[19.] Lin, T., Goyal, P. and Girshick, R. (2020) 'Focal loss for dense object detection', *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 42(2), pp. 318-327.

[20.] Kingma, D. and Ba, J. (2015) 'Adam: A method for stochastic optimization', *Proceedings of the International Conference on Learning Representations (ICLR)*.