Infrared Clues That Help Track Lupus Nephritis Over Time

A label-free infrared method enables clinicians to quickly and precisely track kidney inflammation.

Monitoring lupus nephritis (LN) has long been one of the most difficult challenges in autoimmune medicine. Standard laboratory biomarkers often change too slowly to reflect real-time kidney inflammation, while a kidney biopsy is invasive and unsuitable for frequent monitoring. In response to this gap, a collaborative team led by Mei-Ching Yu (Lin-Kou Chang Gung Memorial Hospital) and Yao-Chang Lee (NSRRC) has developed an innovative infrared (IR) spectroscopic approach that reveals LN activity from a simple drop of serum, without the need for labels or chemical reagents. Their study introduces a practical and patient-friendly tool with the potential to transform how clinicians evaluate disease progression and therapeutic response.[1]

The new method relies on attenuated total reflection Fourier-transform infrared (ATR-FTIR) spectroscopy, performed at the **TLS 14A1** IR beamline. Rather than using only static spectral snapshots, the team monitored how serum IR absorption bands change during a controlled dehydration process. These time-resolved signals contain subtle biochemical information—such as IgG glycosylation, lactate levels, protein hydrophobicity, and albumin content—that closely correlate with LN disease activity. To quantify these changes, the researchers introduced a metric called the Relative Absorption Difference (RAD) and defined a measurable RAD gap, representing the difference between early-stage and late-stage values of each spectral marker during dehydration. **Figure 1** shows how the method captures biochemical fingerprints spanning carbohydrates, amino acids, lipids, and protein backbones. These spectral markers include (1) a glycosylation-related band at 1030 cm^{-1}, (2) a lactate band at 1121 cm^{-1}, (3) protein hydrophobic/hydrophilic signatures near 2930–2960 cm^{-1} and 1546–1650 cm^{-1}, and (4) albumin-related vibrations around 1400–1450 cm^{-1}. When analyzed together, these markers provide a comprehensive, label-free biochemical profile of patient serum.

$$\mathbf{RAD}(\nu_1, \nu_2, t, T) = \frac{\mathbf{PH}_1(\nu_1, t, T) - \mathbf{PH}_2(\nu_2, t, T)}{\mathbf{PH}_1(\nu_1, t, T)}$$

Hydrophobicity (Hp) $\frac{\mathbf{PH}_1(\nu_{as}(CH_2)_{2930}, t, T) - \mathbf{PH}_2(\nu_{as}(CH_3)_{2960}, t, T)}{\mathbf{PH}_1(\nu_{as}(CH_2)_{2930}, t, T)}$	**Hydrophilicity (Hph)** $\frac{\mathbf{PH}_1(AM\ II_{1550}, t, T) - \mathbf{PH}_2(AM\ I_{1650}, t, T)}{\mathbf{PH}_1(AM\ II_{1550}, t, T)}$	**Albumin (Alb)** $\frac{\mathbf{PH}_1(\delta(COO^-)_{1400}, t, T) - \mathbf{PH}_2(\delta(CH_2)_{1450}, t, T)}{\mathbf{PH}_1(\delta(COO^-)_{1400}, t, T)}$
Lactate (Lact) $\frac{\mathbf{PH}_1(\delta(C\text{–}O\text{–}H)_{1121}, t, T) - \mathbf{PH}_2(\delta(C\text{–}O\text{–}H)_{1171}, t, T)}{\mathbf{PH}_1(\delta(C\text{–}O\text{–}H)_{1121}, t, T)}$	**Glycosylation (Gly)** $\frac{\mathbf{PH}_1(\delta(C\text{–}O\text{–}H)_{1030}, t, T) - \mathbf{PH}_2(\delta(C\text{–}O\text{–}H)_{1171}, t, T)}{\mathbf{PH}_1(\delta(C\text{–}O\text{–}H)_{1030}, t, T)}$	**Hydrophobicity Index (HPI)** $\frac{\mathbf{PH}_1(\nu_{as}(CH_2)_{2930}, t, T)}{\mathbf{PH}_2(\nu_{as}(CH_3)_{2960}, t, T)}$

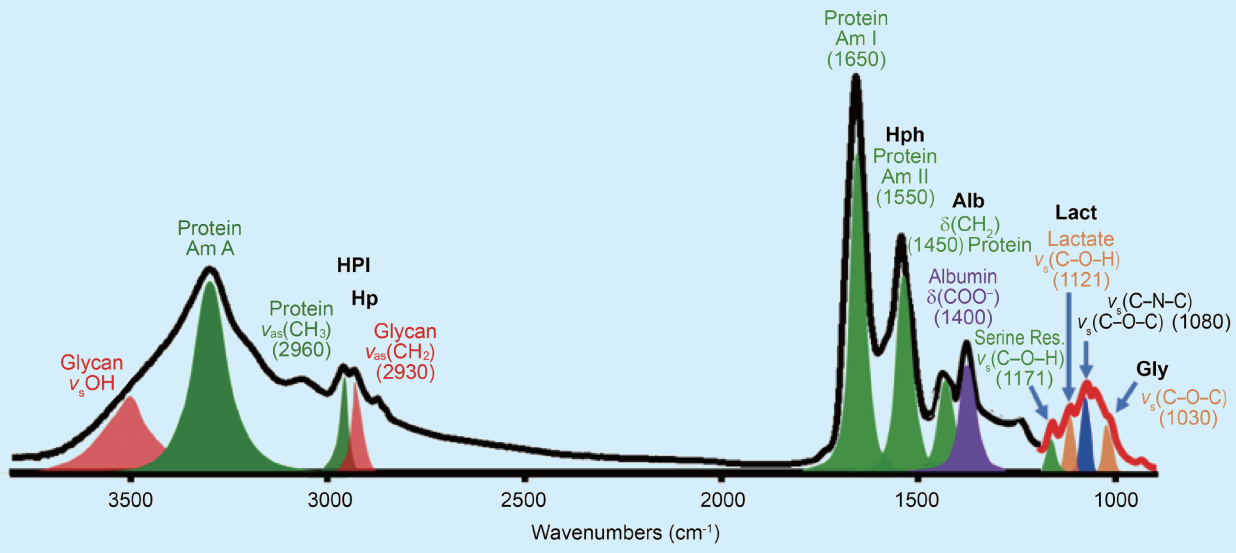

Fig. 1: The RAD equation is determined by five spectral indices (Lactate (Lact), Glycosylation (Gly), Hydrophobicity (Hp), Hydrophilicity (Hph), and Albumin (Alb)) and their respective band assignments. [Reproduced from Ref. 1]

One of the most compelling findings is that RAD gaps correlate strongly with standard clinical indicators such as serum creatinine, urine total protein, and the urine protein-to-creatinine ratio. In acute LN patients, RAD gaps for IgG glycosylation, lactate, and serum hydrophobicity increased during disease flares and decreased as treatment took effect. Conversely, the serum hydrophilicity and albumin RAD gaps displayed opposite trends, mirroring the well-known drop in serum albumin during active inflammation. Because these optical signatures respond rapidly to biochemical changes, they provide a quick, sensitive means to detect early shifts in LN status.

To consolidate all spectral information into a single, clinically relevant score, the team developed iPath software, which calculates the Prognosis Prediction Function from the five RAD gaps. This composite score closely follows patient trajectories—even over more than 700 days of follow-up—and frequently indicates improvement or relapse earlier than conventional laboratory tests. The study highlights that spectral-based indices can assist clinicians in detecting flare-ups, assessing treatment response, and tailoring immunosuppressive regimens.

In addition to IR spectroscopy, the researchers examined the structural consequences of immune activation by analyzing purified IgG samples at the **TPS 13A** biological small-angle X-ray scattering (BioSAXS) beamline. SAXS measurements revealed that IgG molecules from patients with active LN exhibited a larger radius of gyration (Rg), indicating conformational changes likely associated with altered glycosylation patterns. For example, initial samples from an acute LN patient showed Rg values around 57 Å—significantly higher than those measured after remission or in healthy controls (~50 Å). This cross-validation demonstrates a strong link between biochemical IR signatures and macromolecular structural changes, reinforcing the diagnostic value of the RAD-based approach.

The clinical implications are substantial. LN is a heterogeneous disease: two patients with similar biopsy findings may respond very differently to the same therapy. By providing rapid, quantitative, and minimally invasive biochemical readouts, this IR-based assay enables monitoring of each patient's disease status with much greater temporal resolution than current methods. Because ATR-FTIR measurements require only microliters of serum and no additional reagents, the technique is cost-effective and suitable for repeated testing—a key advantage in the long-term management of autoimmune diseases. Furthermore, the underlying principles of the method are generalizable. The RAD framework can be applied to other conditions in which serum composition reflects disease activity, such as metabolic disorders, infections, and inflammatory diseases. The integration of synchrotron IR spectroscopy, chemometric algorithms, and computational enhancement represents an emerging direction in clinical diagnostics, bridging the physics-based measurement with biomedical interpretation.

The collaboration between clinicians and synchrotron scientists demonstrates how advanced photon-based tools can address unmet medical needs. By utilizing the high brilliance and stability of the **TLS 14A1** IR beamline and validating structural signatures with the **TPS 13A** BioSAXS beamline, the team developed a multimodal platform that captures both molecular composition and macromolecular structure. This work highlights NSRRC's expanding role in translational research and precision health technologies. (Reported by Orion Shih)

*This report features the work of Mei-Ching Yu and her collaborators published in Biosensors **15**, 39 (2025).*

TPS 13A Biological Small-angle X-ray Scattering
TLS 14A1 IR Microscopy

- FTIR, SAXS
- Biomedical Science, Biophysics, Structural Biology, Analytical Chemistry

Reference

1. M.-C. Yu, X.-D. Huang, C.-W. Kuo, K.-F. Zhang, P.-C. Liang, U.-S. Jeng, P.-Y. Huang, F.W.K. Tam, Y.-C. Lee, Biosensors **15**, 39 (2025).