# National Magnetic Resonance Facility at Madison (NMRFAM)

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# NMRFAM offers "end-to-end" biomolecular NMR support

## *collaborators/users select only what is needed*

- Experiment design (advice/preliminary data for grant applications)
- Preparation of labeled proteins
- Design of media for residual dipolar coupling measurements
- Software tools for data collection and analysis
- Assistance with experiments
  - Pulse sequence design
  - Setting up data collection (for local or remote use)
  - Data collection
  - Data analysis
  - Manuscript preparation
- Hands-on training

# NMRFAM demographics

- **Equipment use**

  168 Laboratories from 27 states and 4 foreign countries

  92 Persons trained “hands-on” in use of equipment

- **Publications**

  > 40 publications / year (over the past 5 years)

- **Training**

  ~ 23 / year in short course for beginners

  ~ 14 / year in short course on advanced topics

  Tutorials: >9,000 views in past year

- **Software use**

  Worldwide; tracked in various ways

# Infrastructure required of an effective facility

- Administration: reviewing proposals, scheduling, accounting
- Routine maintenance
- Trouble-shooting and repairs
- Technology development to keep up with the field and push boundaries

## Focus at NMRFAM

- Streamlining and automation of routine studies of proteins and RNA molecules
- Improved approaches for large biomolecules and complexes (molecular machines)
- Metabolomics, ligand screening, and natural products

# Academic software for biomolecular NMR: A—to—X

| Software | Category |
|---|---|
| ADAPT-NMR | Automated protein data collection and assignment |
| AMBER | Molecular dynamics with NMR restraints |
| ARIA | Structure determination and refinement |
| CCPN | Data modeling, spectral analysis, format conversion, software integration |
| CING | Structure validation |
| CS23D | Structure determination from chemical shifts |
| CNS | Structure determination |
| CS-Rosetta | Structure determination from chemical shifts |
| CYANA | Automated assignment and structure determination |
| FLYA | Automated assignment and structure determination |
| HADDOCK | Docking |
| MolProbity | Structure analysis and validation |
| NMR-Pipe | Data processing and analysis |
| NMRDRAW | Spectra visualization |
| NMRVIEW | Data analysis |
| Sparky → NMRFAM-SPARKY | Data modeling, spectral analysis, format conversion, software integration |
| PINE | Protein assignments from peak lists |
| PONDEROSA | Structure determination from assignments and NOE data |
| PSVS and PDBStat | Structure validation |
| PyMol | Structure visualization |
| rNMR | Metabolomics |
| TALOS versions | Backbone torsion angles from chemical shifts |
| UNIO | Automation from spectral acquisition to structure |
| XPLOR-NIH | Structure determination and refinement |

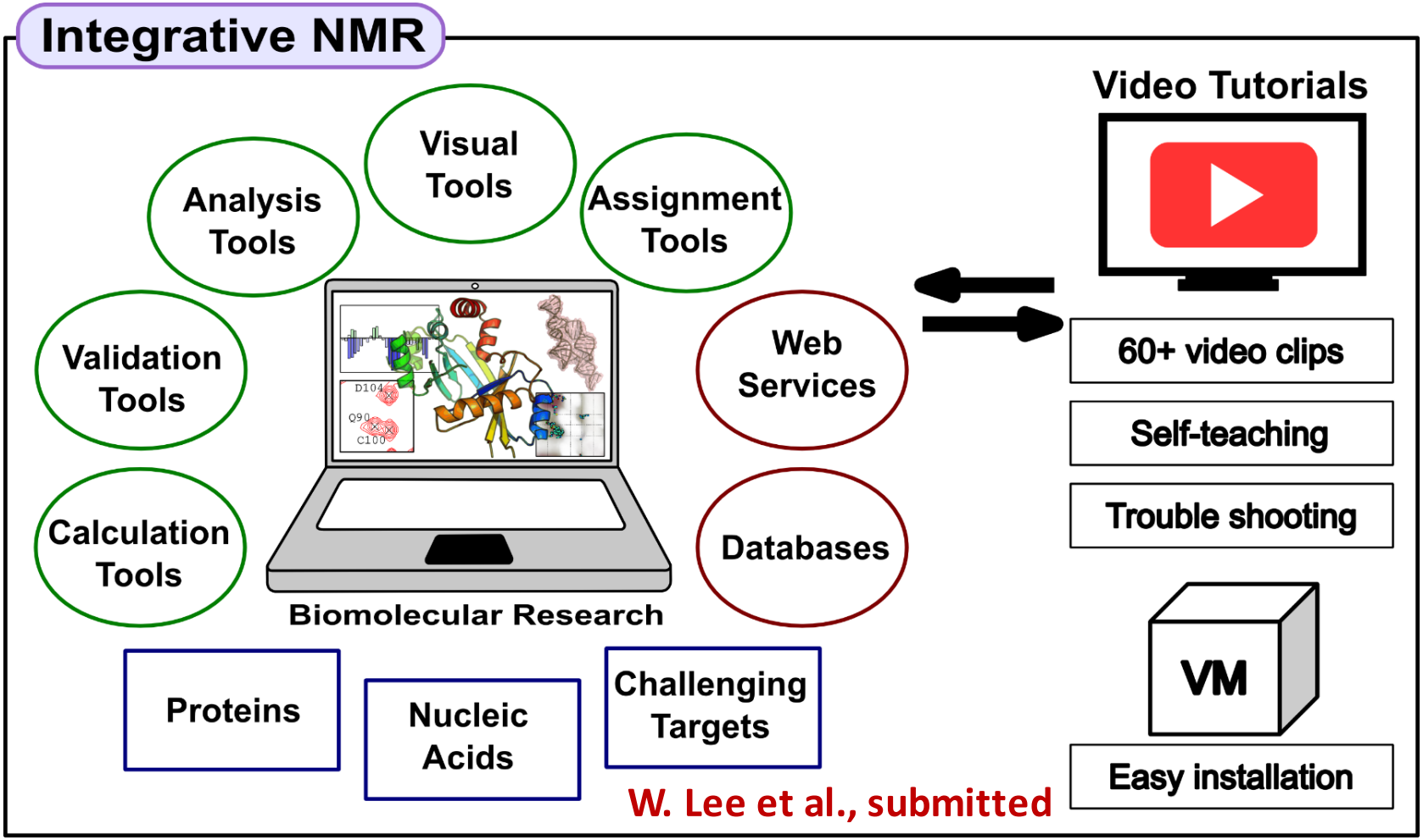
Partial list from the 258 software packages listed as accompanying BMRB depositions

Top 10 in red

# Software challenges

- How to choose packages (functional overlap)
- Lack of documentation and tutorials
- Multiple operating systems and flavors of software (e.g., Java)
- Lack of format standardization (being addressed by wwPDB NEF TF)
  - Atom nomenclature
  - Restraint definition
- Lack of interoperability (being addressed by wwPDB NEF TF)
  - Conversion of data from one software package to another
  - Conversion to and from the archival format (NMR-STAR)

# NMRFAM approach: bundling of interactive tools covering the biomolecular NMR workflow in a virtual machine that allows seamless interaction with web services and databases



# Archiving for data sharing and experiment reproducibility

- **Hybrid approaches** are the way of the future

  NMR, X-ray, CryoEM, SAXS, WAXS, FRET, crosslinking, …

- **Federated database** effort underway, led by wwPDB (Worldwide Protein Data Bank)

- **wwPDB structural archive** includes: X-ray, EM, NMR

  Data format: mmCIF (= PDBx)

- **NMR experimental archive**: BMRB (Biological Magnetic Resonance data Bank)

  Data format: NMR-STAR (interconvertible with mmCIF)

- **Data validation and reproducibility** are of primary importance

# Thanks!