Quadrupolar NMR in Biology (1982-89). In early years, Tsai has pioneered the use of ^{17}O NMR and other quadrupolar NMR such as ^{25}Mg NMR, ^{2}H NMR, ^{43}Ca NMR, in enzymology and in metal-nucleotide interactions. He has also written several book chapters on the usage of these NMR methods in enzyme mechanisms. After spending a sabbatical year with John Markley at Wisconsin in 1989, his interest in NMR has turned into solving protein structures by high-resolution NMR as described in later sections. Publications: #20, 21, 27, 28, 36, 43, 44, 56.

1. "Does Mg^{2+} Interact with the a-Phosphate of ATP? An Investigation by ^{17}O NMR," S.-L. Huang and M.-D. Tsai, *Biochemistry 21*, 951-959 (1982).

2. "Use of $^{31}P(^{18}O)$, $^{31}P(^{17}O)$, and ^{17}O NMR Methods to Study Enzyme Mechanism Involving Phosphorus," M.-D. Tsai, *Methods Enzymol. 87*, 235-279 (1982).

3. "Effects of ^{17}O and ^{18}O on ^{31}P NMR: Further Investigation and Applications," R. D. Sammons, P. A. Frey, K. Bruzik and M.-D. Tsai, *J. Am. Chem. Soc. 105*, 5455-5461 (1983).

4. "NMR Methods Involving Oxygen Isotopes in Biophosphates," M.-D. Tsai and K. Bruzik, in *Biological Magnetic Resonance*, Vol. 5, L. J. Berliner and J. Reuben, Eds., Plenum Press, New York, pp. 129-181 (1983).

5. "Metal-Nucleotide Interactions. 3. ^{17}O, ^{31}P and ^{1}H NMR Studies on the Interactions of Sc(III) and La(III) with ATP," Y.-J. Shyy, T.-C. Tsai and M.-D. Tsai, *J. Am. Chem. Soc. 107*, 3478-3484 (1985).
6. "Is the Binding of Mg^{2+} to Calmodulin Significant? An Investigation by ^{25}Mg NMR," M.-D. Tsai, T. Drakenberg, E. Thulin and S. Forsen, *Biochemistry, 26*, 3635-3643 (1987).

7. "Magnesium Binding to Calcium-Binding Proteins: A Regulatory Function?" T. Drakenberg, S. Forsen, E. Thulin, and M.-D. Tsai, in *Calcium-Binding Proteins in Health and Disease*, Norman, A. W., Vanaman, T. C., and Means, A. R., Eds., Academic Press, pp. 430-432 (1987).

8. "Ligand-Protein Interactions Via NMR of Quadrupolar Nuclei". C. R. Sanders II and M.-D. Tsai, *Methods. Enzymol. 177*, 317-333 (1989).