# This Week's Citation Classic

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**Noll M.** Subunit structure of chromatin. *Nature* **251**:249-51. 20 September 1974.
[MRC Laboratory of Molecular Biology, Cambridge, England]


**Evidence in favor of a subunit structure of chromatin is presented. The subunit is shown to contain about 200 base pairs of DNA and has been isolated by sedimentation through a sucrose gradient. As well as demonstrating the existence of a chromatin subunit, the methods described provide a means of isolating the subunit on a preparative scale and represent a test for chromatin structure. [The *SCI*® indicates that this paper has been cited in over 635 publications since 1974.]**



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"When I joined the small group working on chromatin at the Medical Research Council in Cambridge in 1973, I first discovered that the little I knew about chromatin was probably wrong. I arrived just in time for the annual lab lectures held during the first week of October. Although the lectures were captivating, covering a wide spectrum of biological structures, chromatin appeared to receive relatively little attention. However, this impression was deceiving as I soon learned from Francis Crick and Roger Kornberg at lunch. Roger proposed that chromatin is built on repetitive structural units of 200 base pairs of DNA and two each of the histones H2A, H2B, H3, and H4.[1]

"Because of its simplicity, the model was very appealing. It was consistent with experiments of Kornberg and Thomas on histone-histone interactions[2] and with results of Hewish and Burgoyne, who reported that DNA in rat liver nuclei was cleaved by an endogenous nuclease at sites multiples of a unit length apart. [3] On the other hand, the model seemed to be in conflict with the literature claiming that the four main types of histones did not occur in a simple stoichiometric relationship

"After I had confirmed the result of Hewish and Burgoyne,[3] I started to purify the endogenous nuclease from rat liver. Soon, however, I realized that for any structural studies on a large scale, the amount of enzymatic activity that could be obtained was too small. In the hope that commercially available nucleases recognize the presumptive subunit structure, I tested DNase I and micrococcal nuclease which were in stock at the lab's stores. Whereas results obtained with DNase I were disappointing at first, micrococcal nuclease did indeed cleave chromatin at regularly spaced sites. Using this nuclease, I could demonstrate that at least 87 percent of rat liver chromatin consists of the proposed subunit structure and that the DNA length per subunit is 200 base pairs Furthermore, I was able to isolate single subunits (later called nucleosomes) and define lengths of oligonucleosomes by sedimentation through sucrose gradients and thus provide the basis for detailed structural studies dependent on preparative amounts of nucleosomes.[4] Digestion with DNase I produced an equally startling result when the DNA fragments were analyzed in their single-stranded form in denaturing gels.[5] In contrast to micrococcal nuclease, DNase I cleaved the DNA within nucleosomes at sites spaced by the pitch of the DNA which was consistent with its regular arrangement on the outside of the histone core.[5] Digestion with either nuclease represented simple tests for chromatin structure which have since been used frequently.[6]

"The paper has probably been cited mainly for three reasons: it was the first demonstration of a well-defined subunit structure of chromatin as it had been proposed by Kornberg,[1] it described a method for the isolation of the subunits on a preparative scale, and it provided a test for chromatin structure. The work was honored by the Friedrich Miescher Award in 1978 "


1 **Kornberg R D.** Chromatin structure: a repeating unit of histones and DNA. *Science* **184**:868-71, 1974.
2. **Kornberg R D & Thomas J O.** Chromatin structure: oligomers of the histones. *Science* **184**:865-8. 1974.
3. **Hewish D R & Burgoyne L A.** Chromatin sub-structure. The digestion of chromatin DNA at regularly spaced sites by a nuclear deoxyribonuclease. *Biochem. Biophys Res Commun.* **52**:504-10. 1973.
[Citation Classic. *Current Contents/Life Sciences* **25**(5):20. 1 February 1982.]
4. **Finch J T, Luller L C, Rhodes D, Brown R S, Rushton B, Levitt M & Klug A.** Structure of nucleosome core particles of chromatin. *Nature* **269**:29-36. 1977.
5. **Noll M.** Internal structure of the chromatin subunit. *Nucl. Acid. Res.* **1**:1573-8. 1974.
6 **Igo-Kemenes T, Hörz W & Zachau H G.** Chromatin. *Annu. Rev Biochem.* **51**:89-121. 1982.