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Virus disinfection mechanisms: the role of virus composition, structure, and function
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Drinking waters are treated for enteric virus via a number of disinfection techniques including chemical oxidants, irradiation, and heat, however the inactivation mechanisms during disinfection remain elusive. Owing to the fact that a number of significant waterborne virus strains are not readily culturable in vitro at this time (e.g. norovirus, hepatitis A), the susceptibility of these viruses to disinfection is largely unknown. An in-depth understanding of the mechanisms involved in virus inactivation would aid in predicting the susceptibility of non-culturable virus strains to disinfection and would foster the development of improved disinfection methods. Recent technological advances in virology research have provided a wealth of information on enteric virus compositions, structures, and biological functions. This knowledge will allow for physical/chemical descriptions of virus inactivation and thus further our understanding of virus disinfection to the most basic mechanistic level.

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Introduction
Obtaining a mechanistic understanding of virus disinfection is a pressing need in environmental engineering owing to the enduring occurrence of waterborne and food-borne virus outbreaks. Many important enteric viruses remain non-culturable to date (e.g. norovirus, hepatitis A); therefore, their susceptibility to disinfection cannot be experimentally tested. Non-culturable virus disinfection kinetics must be either determined with human charge studies or predicted using surrogate viruses that can be cultured in vitro but that differ in composition, structure, and function. A framework that enables the accurate prediction of virus inactivation behavior based on a detailed understanding of the processes involved would assist in the development of effective disinfection strategies.

Scientists have long sought to provide mechanistic descriptions of virus inactivation during drinking water disinfection [1]. In the 1960–1980s, researchers employed scintillation spectroscopy and electron microscopy techniques to detect modifications in viral genomes and proteins and typically reported one of two conclusions: 1) inactivation is the result of damage to the virus proteins or 2) inactivation is the result of damage to the genome [2–6]. Although these early studies investigated the molecular mechanisms as much as technologically possible, more recent research has focused less on elucidating mechanisms and more on comparing inactivation kinetics with various virus strains, disinfectants, and water chemistries [7–9]. This is despite the fact that recent technological advances have provided improved tools for probing molecular mechanisms. Collectively, the proposed virus inactivation mechanisms by common water disinfectants vary widely and are often contradictory. For example, the inactivation of poliovirus by chlorine has been attributed to RNA degradation [2] and to capsid protein modifications [10]. At this time, the fundamental questions of what modifications do or do not cause inactivation remain elusive.

Herein, we discuss how the combined knowledge of virus composition, structure and biological function will further our understanding of virus disinfection at the most basic mechanistic level. A physical/chemical description of inactivation is more feasible today than it was ten years ago thanks to advances in genome sequencing, protein mass spectrometry, and structural virology techniques. We focus the majority of our discussion on the disinfection of waterborne enteric viruses [11], in general, and poliovirus, in particular. Enteric viruses are the most relevant to water treatment and poliovirus has been the focus of numerous disinfection studies over the past several decades [12–14]. It should be noted that this discussion could be extrapolated to other settings where disinfection is used to mitigate virus transmission, such as food safety or medical equipment sterilization.

Bottom-up approach to describe virus reactivity: composition only
The reactions that take place between amino acid or nucleotide monomers and common water disinfectants
such as chlorine, ozone, or UV irradiation are fairly well characterized (Table 1). Consequently, established reaction rate constants for amino acid and nucleotide monomers can be summed based on their known abundance within virus particles to provide predictions of the relative reaction rates of genome and protein targets [15]. When this is done for Poliovirus 1 Mahoney, chemical disinfectants such as chlorine and ozone are much more reactive with viral protein material than with genomic material (Figure 1). On the contrary, UVC radiation affects the genomic material more than the protein material. Unfortunately, such predictions are inaccurate owing to the influence of protein and genome higher-level organization on reaction rates [16–18]. For example, when treated with chlorine dioxide, denatured poliovirus genomes degraded at a different rate than native poliovirus genomes [19*]. Reactions that take place in the genome and proteins during disinfection can form byproducts that further react with amino acids and nucleotides [20]; this makes reactivity predictions even more complicated.

Unlike chemical oxidants, UVC radiation will lead to direct photolysis of photolabile virus components regardless of their solvent accessibility. A genome-size based approach to predict the sensitivity of virus strains to UVC has been proposed [21], although others have reported that genome-size does not always correlate with virus susceptibility to UV disinfection [22,23]. Similar to the genome-size based approach, pyrimidine doublet prevalence in virus genomes was suggested as a framework to predict UVC susceptibility [24*]. Indeed, a plot of the number of potential dimerization sequences in a virus genome versus effective UV dose suggested a correlation. The presence of outlier virus strains, however, indicates that alternative pathways play a role in some UV inactivation mechanisms. Taken together, these discrepancies demonstrate that virus component information (i.e. genome and protein sequences) alone will not allow for an accurate prediction of susceptibility. A prior knowledge of capsid and genome structure should therefore aid in interpreting and predicting virus particle reactivity and in identifying the particle’s most susceptible regions.

![Figure 1](Current Opinion in Virology 2012, 2:84–89)
Coupling structure and composition information aids in our understanding of virus reactivity

X-ray crystal structures have been published for numerous enteric viruses [25,26,27] and with these reports have come a windfall of valuable information including the location and orientation of capsid protein residues. Cryo-electron microscopy (cryoEM) has expanded our knowledge of virus structures even further, as it allows virologists to study virus particles that are difficult to crystallize due to either complex capsid shapes, inadequate purification, or intermediate, metastable structures (e.g. virus binding or cell entry processes [28,29]). In fact, recent advances in cryoEM have lead to viral reconstructions at resolutions comparable to those obtained with X-ray crystallography [30,31]. In addition to ordered capsid protein visualization, cryoEM studies have demonstrated that some viruses have ordered genomes [32] and have described specific interactions between capsid proteins and packaged genomes [33]. It should be noted that resolved near-atomic structures are not yet available for some important enteric viruses such as hepatitis A and human norovirus, although recombinant norovirus-like particles have been reconstructed [34].

Some caution must be taken when using virus structural data to identify the location and solvent accessibility of functional groups. Virus capsids can be fluid in nature and thus functional groups that are normally protected from oxidants in the solvent can be periodically exposed to the capsid surface [35]. In human rhinovirus, for example, certain regions are static and in agreement with the crystal structure, while other regions are more fluid [36].

Together, composition data and structure data will provide an improved framework to describe the reactivity of virus components with disinfectants. Indeed, a number of studies on nonviral proteins have used structural data to explain the site-specific reactivity of protein components [16,17,37,38]. At this time, however, only a few reports on virus disinfection have mentioned resolved virus structures in the interpretation of results [10,39,40]. A study on adenovirus inactivation with chlorine did employ adenovirus structural data to suggest that damaged Met or His residues near a critical motif may contribute to inactivation [39]. In another study, protein mass spectrometry was used to identify specific residues in MS2’s capsid proteins as the virus was inactivated by UV [25] and singlet oxygen [40]. Residues on the outside surface of the capsid were modified with O2 treatment while residues on the inside surface of the capsid near the viral genome were modified with UV treatment. More research is clearly needed to elucidate the effect of virus structure on the reactivity of virus components.

Knowledge of virus functions is required to understand and predict inactivation mechanisms

Composition and structure information aids in describing where modifications are most likely to occur in a virus particle during disinfection; however, modifications do not always cause inactivation. For example, although ozonation of poliovirus altered viral proteins VP1 and VP2, inactivation was ultimately attributed to genome damage [5]. Solely identifying susceptible virus regions based on composition and structure will be insufficient to describe and predict the effect of a disinfectant on virus infectivity. One must also consider the effect that particular modifications have on fundamental virus functions (e.g. host-cell binding, genome entry, etc.). In order to do this, the fundamental functions and virus components involved in those functions must be well defined.

Virus structural and dynamic information has provided an improved understanding of the biological function of viral domains, including virus–host cell interaction [26,41], virus assembly [26], capsid-RNA interaction sites [33,42] and RNA release [42] and references therein). This new knowledge provides valuable insight into critical structures and biological functions of the virus and thus identifies regions and functions that should be targeted in virus neutralization or inactivation strategies.

The promise of a structure/function-based approach for disinfection is underscored by the fact that the medical field has exploited this method to develop vaccines [41] and antiviral drugs [43] as well as to better understand the mechanism of previously developed vaccines [41]. This type of approach has great benefits over the traditional method of screening and isolating fortuitously emerged, non-virulent virus strains or neutralizing antibodies. Namely, it enables the rational design of site-specific antivirals and vaccines that target relevant virus structures common to several strains or species. For example, coronavirus strains were long believed to have host receptors that were too diverse and too prone to mutation to be susceptible to a broad-spectrum antiviral. Recently, however, Yang et al. [44] used function and structure information of all three genetic coronavirus clusters to determine that the main protease has a highly conserved substrate-recognition pocket. Based on this structural information combined with compositional information of conserved amino acids within this region, a protease inhibitor was designed that successfully prevented virus replication of two coronaviruses. Ultimately, the authors suggest that the knowledge of the conserved structure and biochemistry of the protease will lead to the development of a single, broad spectrum antiviral that targets all coronaviruses. A similar approach to water disinfection will lead to the rational design of novel disinfectants.
Towards a predictive model for virus susceptibility and disinfection kinetics

An important difference between water disinfection and antiviral drugs, however, is that traditional disinfection does not operate by physically blocking a virus site or particular function via the addition of an external chemical or antibody, but by chemically or structurally altering one or several important sites. We therefore expect that the intrinsic reactivities of the various virus components are of greater importance to disinfection than to drug development. As discussed above, this intrinsic reactivity is dictated by both specific chemical composition and the structure. As such, the structure/function approach used in the medical field would have to be expanded to a composition/structure/function approach in water treatment.

As an example of how structural commonalities and compositional differences may be used to predict susceptibilities to disinfectants, we look at poliovirus 1 Brunhilde and poliovirus 1 Mahoney. The Brunhilde strain was reported to be twice as resistant to chlorination as the Mahoney strain [45,46]. This discrepancy in inactivation kinetics is intriguing as the two strains have nearly identical capsid protein sequences (~98%) and have similarly sized genomes. Inactivation of the Mahoney strain by chlorine was attributed to a loss in ability to attach to the host cell [10], however this has not been examined for the Brunhilde strain. CryoEM analysis has provided a three-dimensional structure of the poliovirus particle bound to its host cell receptor, sPvr [47], and a number of capsid protein residues were implicated in the virus capsid-host cell interaction. Interestingly, six of these implicated residues differ in the Mahoney and Brunhilde strains, including Mahoney VP2 Met140 (Thr in Brunhilde) and His141 (Tyr in Brunhilde) (Figure 2). Methionine and histidine side chains readily react with chlorine; threonine and tyrosine sidechains, on the contrary, are much less reactive. It is thus possible that the lack of Met and His residues at the binding site is responsible for the greater resistance of the Brunhilde strain to chlorine disinfection.

This is only a hypothetical explanation and will need to be confirmed through experimentation; it does, however, demonstrate the manner in which composition, structure, and function information can assist in deducing virus inactivation mechanisms. It also demonstrates how such knowledge aids in predicting how a new strain will behave based on mutations in the binding site. Suppose, for example, a new poliovirus strain emerges with fewer reactive functional groups in its binding site. The new strain would be expected to be more resistant to disinfection than the well-characterized strain. For fast-mutating viruses like human norovirus, this type of predictive tool would be particularly valuable. Research is needed to assess exactly how similar virus strains should be in structure, composition, and function for such a predictive tool to work.

Conclusions and future prospective

To reach a point where a holistic understanding of virus inactivation is in hand, a number of questions will first need to be addressed. Specific questions include: 1) Which virus protein residues are involved with fundamental functions and how do these vary amongst different strains and species; 2) What specific chemical modifications take place in the genome and capsid during disinfection and what effects do these modifications have on virus structure and function; 3) How similar are disinfectant-induced modifications amongst various enteric viruses? Answering these questions is a lofty goal given the numerous virus-disinfectant pairs that will need to be examined.

In conclusion, the study of virus fate in water treatment is entering an exciting new phase thanks to the advent of tools that provide insight into virus structure and function. As a result, virus inactivation predictive tools and the design of highly efficient disinfectants may be a reality in the not-so-distant future.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest
Thurman RB, Gerba CP: Molecular mechanisms of viral inactivation by water disinfectants. Adv Appl Microbiol 1988, 33:79-105.

2. Obrien RT, Newman J: Structural and compositional changes associated with chlorine inactivation of polioviruses. Appl Environ Microbiol 1979, 38:1034-1039.

3. Dennis WH, Olivieri VP, Kruse CW: Mechanism of disinfection – incorporation of Cl– into F2 virus. Water Res 1979, 13:363-369.

4. Kim CK, Gentile DM, Sproul OJ: Mechanism of ozone inactivation of bacteriophage-F2. Appl Environ Microbiol 1980, 39:210-218.

5. Roy D, Wong PK, Engelbrecht RS, Chian ES: Mechanism of enteroviral inactivation by ozone. Appl Environ Microbiol 1981, 41:718-723.

6. Alvarez ME, O’Brien RT: Mechanisms of inactivation of poliovirus by chlorine dioxide and iodine. Appl Environ Microbiol 1992, 44:1064-1071.

7. Kahler AM, Cromeans TL, Roberts JM, Hill VR: Effects of source water quality on chlorine inactivation of adenovirus, coxsackievirus, echovirus, and murine norovirus. Appl Environ Microbiol 2010, 76:5159-5164.

8. Cromeans TL, Kahler AM, Hill VR: Inactivation of adenoviruses, enteroviruses, and murine norovirus in water by free chlorine and monochloramine. Appl Environ Microbiol 2010, 76:1028-1033.

9. Thurston-Enriquez JA, Haas CN, Jacangelo J, Gerba CP: Inactivation of enteric adenovirus and feline calicivirus by chlorine dioxide. Appl Environ Microbiol 2005, 71:3100-3105.

10. Nuanualsawan S, Oliver DP: Capsid functions of inactivated human picornaviruses and feline calicivirus. Appl Environ Microbiol 2003, 69:350-357.

11. Carter MJ: Enterically infecting viruses: pathogenicity, transmission and significance for food and waterborne infection. J Appl Microbiol 2005, 98:1354-1380.

12. Floyd R, Johnson JD, Sharp DG: Inactivation by bromine of single poliovirus particles in water. Appl Environ Microbiol 1976, 31:298-303.

13. Payment P, Tremblay M, Trudel M: Relative resistance of chlorine to poliovirus and coxsackievirus isolates from environmental sources and drinking water. Appl Environ Microbiol 1985, 49:981-983.

14. Shin G, Sobsey MD: Reduction of Norwalk virus, poliovirus 1, and bacteriophage MS2 by ozone disinfection of water. Appl Environ Microbiol 2003, 69:3975-3978.

15. Davies MJ: Singlet oxygen-mediated damage to proteins and its consequences. Biochem Biophys Res Commun 2003, 305:761-770.

16. Kim J, Rodriguez ME, Guo M, Kenney ME, Oleinick NL, Anderson VE: Oxidative modification of cytochrome c by singlet oxygen. Free Radic Biol Med 2008, 44:1700-1701.

17. Michaël A, Feitelson J: Reactivity of singlet oxygen toward proteins: the effect of structure in basic pancreatic trypsin inhibitor and in ribonuclease A. Photochem Photobiol 1997, 65:309-315.

18. Saito I, Takayama M, Sugiyama H, Nakatani K: Photoinduced DNA cleavage via electron transfer: demonstration that guanine residues located 5‘ to guanine are the most electron-donating sites. J Am Chem Soc 1995, 117:6406-6407.

19. Simonet J, Gantzer C: Degradation of the Poliovirus 1 genome by chlorine dioxide. J Appl Microbiol 2006, 100:862-870.

20. Pattison DL, Hawkins CL, Davies MJ: Hypochlorous acid-mediated protein oxidation: how important are chlorine transfer reactions and protein tertiary structure? Biochemistry 2007, 46:9853-9864.

21. Lytle CD, Sagripani JL: Predicted inactivation of viruses of relevance to biodefense by solar radiation. J Virol 2005, 79:14244-14252.

22. Sommer R, Pribil W, Appelt S, Gehring P, Eschweiler H, Leth H, Cabaj A, Haider T: Inactivation of bacteriophages in water by means of non-ionizing (UV-253.7 nm) and ionizing (gamma) radiation: a comparative approach. Water Res 2001, 35:3109-3116.

23. Simonet J, Gantzer C: Inactivation of poliovirus 1 and F-specific RNA phages and degradation of their genomes by UV irradiation at 254 nanometers. Appl Environ Microbiol 2006, 72:7671-7677.

24. Kowalski W, Bahnfleth W, Hernandez M: A genomic model for predicting the ultraviolet susceptibility of viruses. IVJU News 2009, 11:15-28.

This study proposed a mathematical model to predict the susceptibility of viruses to inactivation by UVDis. The model was based on the prevalence of viral genome sequences that readily undergo dimerization with UV radiation.

25. Hendry E, Hatanaka H, Fry E, Smyth M, Tate J, Stanway G, Santti J, Maaronen M, Hyypia T, Stuart D: The crystal structure of coxsackievirus A9: new insights into the uncoating mechanism of Enteroviruses. Structure 1999, 7:1527-1538.

26. Yamashita T, Mori Y, Miyazaki N, Chen RH, Yoshimura M, Unno H, Shimma R, Morishita K, Tsukihara T, Li TC et al.: Biological and immunological characteristics of hepatitis E virus-like particles based on the crystal structure. Proc Natl Acad Sci USA 2009, 106:12986-12991.

This research solved the first crystal structure of hepatitis E virus-like particles at 3.5 Å resolution and identified a putative cellular binding region in the capsid via mutational analyses.

27. Reddy VS, Natchiar SK, Stewart PL, Nemirov GR: Crystal structure of human adenovirus at 3.5 Å resolution. Science 2010, 329:1071-1075.

28. Zhang X, Jin L, Fang G, Wong HH, Zhou ZH: 3.3 Å cryo-EM structure of a nonenveloped virus reveals a priming mechanism for cell entry. Cell 2010, 141:472-482.

29. Fu C, Johnson JE: Viral life cycles captured in three-dimensions with electron microscopy tomography. Curr Opin Virol 2011, 1:9-9.

An effective review of recent electron cryotomography studies that have elucidated the complex structure and life cycles of viruses.

30. Zhang X, Settembre E, Xu C, Dormitzer PR, Bellamy R, Harrison SC, Gregoire N: Near-atomic resolution using electron cryo-tomography and single-particle reconstruction. Proc Natl Acad Sci USA 2005, 102:1867-1872.

31. Hryc CF, Chen D-H, Chiu W: Near-atomic resolution cryo-EM for molecular virology. Curr Opin Virol 2011, 1:110-117.

A review highlighting several recent cryo-EM virus studies and the novel insights they have provided.

32. Prasad BVV, Rothnagel R, Zeng C, Jakana J, Lawton JA, Chiu W, Estes MK: Visualization of ordered genomic RNA and localization of transcriptional complexes in rotavirus. Nature 1996, 382:471-473.

33. Pan J, Dong L, Lin L, Ochoa WF, Sinkovits RS, Havens WM, Nibert ML, Baker TS, Shabbir SA, Tao YJ: Atomic structure reveals the unique capsid organization of a dsRNA virus. Proc Natl Acad Sci USA 2009, 106:4225-4230.

34. Prasad BVV, Hardy ME, Dokland T, Bella J, Rossmann MG, Estes MK: X-ray crystallographic structure of the Norwalk virus capsid. Science 1999, 286:287-290.

35. Broo K, Wei J, Marshall D, Brown F, Smith TJ, Johnson JE, Schneemann A, Slusdak G: Viral capsid mobility: a dynamic conduit for inactivation. Proc Natl Acad Sci USA 2001, 98:2274-2277.

This study provided evidence that virus inactivation by small alkylation agents is due to reactions in the viral genome; it therefore demonstrated that certain chemicals can diffuse through virus protein capsids even when the capsids are void of holes or major crevices.
36. Wang L, Smith DL: Capsid structure and dynamics of a human rhinovirus probed by hydrogen exchange mass spectrometry. Protein Sci 2005, 14:1661-1672.

37. Szuchman-Sapir AJ, Pattison DI, Ellis NA, Hawkins CL, Davies MJ, Witting PK: Hypochlorous acid oxidizes methionine and tryptophan residues in myoglobin. Free Radic Biol Med 2008, 45:789-798.

38. Szuchman-Sapir AJ, Pattison DI, Ellis NA, Hawkins CL, Davies MJ, Witting PK: Site-specific hypochlorous acid-induced oxidation of recombinant human myoglobin affects specific amino acid residues and the rate of cytochrome b5-mediated heme reduction. Free Radic Biol Med 2010, 48:35-46.

39. Page MA, Shisler JL, Marinis BJ: Mechanistic aspects of 
   adenovirus serotype 2 inactivation with free chlorine. Appl Environ Microbiol 2010, 76:2946-2954.

This study examined the mechanisms responsible for Adenovirus type 2 inactivation with free chlorine disinfection. Inactivation was attributed to damage in virus proteins that control functions post host cell attachment.

40. Wigginton KR, Menin L, Montoya JP, Kohn T: Oxidation of virus proteins during UV 254 and singlet oxygen mediated inactivation. Environ Sci Technol 2010, 44:5437-5443.

This study used protein mass spectrometry to detect modifications in virus capsid proteins as virus were inactivated and demonstrated that singlet oxygen and UVC affect different virus components.

41. Hashiguchi T, Kajikawa M, Maita N, Takeda M, Kuroki K, Sasaki K, Kohda D, Yanagi Y, Maenaka K: Crystal structure of measles virus hemagglutinin provides insight into effective vaccines. Proc Natl Acad Sci USA 2007, 104:19535-19540.

This study solved the crystal structure of measles virus hemagglutinin—the attachment protein responsible for virus entry into the host cell and a target for neutralizing antibodies. The authors suggested that the solved molecular structure can aid in structure-based measles vaccine development.

42. Levy HC, Bostina M, Filman DJ, Hogle JM: Catching a virus in the act of RNA release: a novel poliovirus uncoating intermediate characterized by cryo-electron microscopy. J Virol 2010, 84:4426-4441.

This study used cryo-EM to characterize the poliovirus 80S particle, believed to be the final capsid structure before the viral genome is released into the host cell. A potential mechanism for viral genome release is proposed based on the 80S particle structure and other reported intermediate structures.

43. Krug RM, Aramini JM: Emerging antiviral targets for influenza A virus. Trends Pharmacol Sci 2009, 30:269-277.

44. Yang H, Xie W, Xue Y, Yang K, Ma J, Liang W, Zhao Q, Zhou Z, Pei D, Ziebuhr J et al.: Design of wide-spectrum inhibitors targeting coronavirus main proteases. PLoS Biol 2005, 3:1742-1752.

Irreversible inhibitors for coronavirus strains were designed using the structure of a conserved substrate-recognition pocket. The results demonstrate that it is possible to develop a single antiviral agent effective against a number of coronavirus strains.

45. Sharp D, Leong J: Inactivation of poliovirus-I (Brunhilde) single particles by chlorine in water. Appl Environ Microbiol 1980, 40:381-385.

46. Floyd R, Sharp DG, Johnson JD: Inactivation by chlorine of single poliovirus particles in water. Environ Sci Technol 1979, 13:438-442.

47. Belnap DM, McDermott BM, Filman DJ, Cheng N, Trus BL, Zuccola HJ, Racaniello VR, Hogle JM, Steven AC: Three-dimensional structure of poliovirus receptor bound to poliovirus. Proc Natl Acad Sci USA 2000, 97:73-78.

The structure of poliovirus type 1 bound to its cellular receptor, sPvr, was determined at 21-A resolution with cryo-EM. Capsid protein residues involved in the poliovirus-sPvr interactions were identified and were in general agreement with previous mutagenesis results.

48. Prutz WA: Hypochlorous acid interactions with thiols, nucleotides, DNA, and other biological substrates. Arch Biochem Biophys 1986, 232:110-126.

49. Ishizaki K, Shinriki N, Ueda T: Degradation of nucleic-acids with ozone. V. Mechanism of action of ozone on deoxyribonucleoside 5'-monophosphates. Chem Pharm Bull 1984, 32:3601-3606.

50. Theruvathu JA, Flyunt R, Aravindakumar CT, von Sonntag C: Rate constants of ozone reactions with DNA, its constituents and related compounds. J Chem Soc Perkin Trans 2 2001:269-274.

51. Du H, Fuh R-CA, Li J, Corkan A, Lindsey JS: PhotochemCAD: a computer-aided design and research tool in photochemistry. Photochem Photobiol 1998, 68:141-142.

52. Middleton CT, de La Harpe K, Su C, Law YK, Crespo-Hernandez CE, Kohler B: DNA excited-state dynamics: from single bases to the double helix. Annu Rev Phys Chem 2009, 60:217-239.

53. Gorner H: Photochemistry of DNA and related biomolecules – quantum yields and consequences of photoionization. J Photochem Photobiol B 1994, 26:117-139.

54. Prutz WA: Interactions of hypochlorous acid with pyrimidine nucleotides, and secondary reactions of chlorinated pyrimidines with GSH, NADH, and other substrates. Arch Biochem Biophys 1998, 332:110-120.

55. Pattison DI, Davies MJ: Absolute rate constants for the reaction of hypochlorous acid with protein side chains and peptide bonds. Chem Res Toxicol 2001, 14:1453-1464.

56. Pryor WA, Giarnaalva DH, Church DF: Kinetics of ozonation. 2. Amino-acids and model compounds in water and comparisons to rates in nonpolar-solvents. J Am Chem Soc 1984, 106:7094-7100.

57. Mihalyi E: Numerical values of absorbances of aromatic amino acids in acid neutral and alkaline solutions. J Chem Eng Data 1968, 13:179-182.

58. Khorseshilova EV, Repyeyev YA, Nikogosyan N: UV photolysis of aromatic amino acids and related dipeptides and tripeptides. J Photochem Photobiol B 1990, 7:159-172.