A COMBINED APPROACH OF ELECTRONIC SPECTROSCOPY AND QUANTUM CHEMICAL CALCULATIONS TO ASSESS MODEL MEMBRANES OXIDATION PATHWAYS

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ELECTRONIC SUPPLEMENTARY INFORMATION

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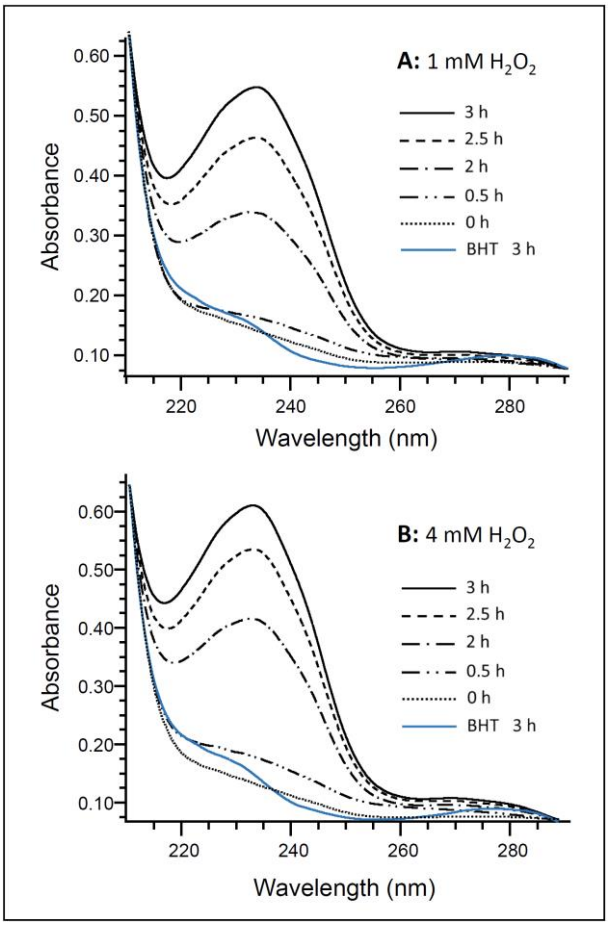
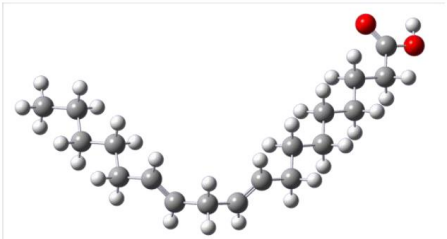
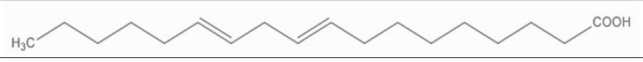
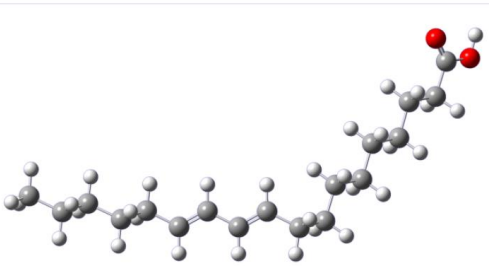
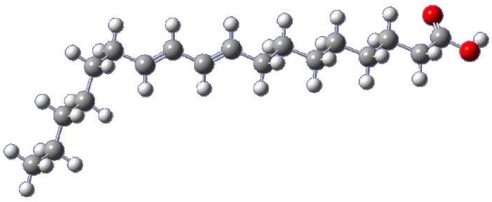


Fig. ESI 1 Raw UV spectra of lipids exposed to H_2O_2 for: 0 hours (dot line); 0.5 hours (dash dot dot line); 2 hours (dash dot line); 2.5 hours (dash line); 3 hours (full line). Blue spectra correspond to liposomes containing BHT and exposed for 3 hours to H_2O_2. A. 1 mM H_2O_2; B. 4 mM H_2O_2.

Proposed pathways [a]	Compounds	Structure
Initial compound	LA	 
A	M	 
	N	 

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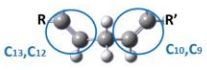
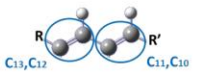
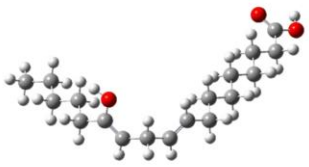
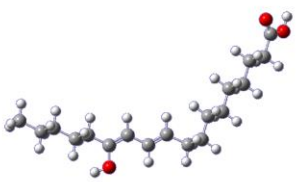
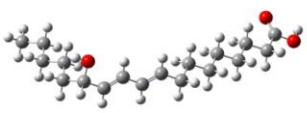
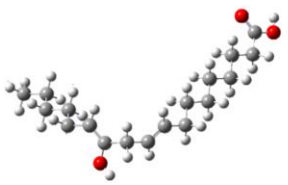
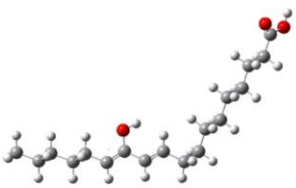
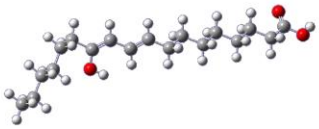
Proposed pathways [a] / Double bond localization		Structure		
				
B	Compounds	A	E	I
	Pathway 1	 	 	 
	Compounds	B	F	J
	Pathway 2	 	 	 

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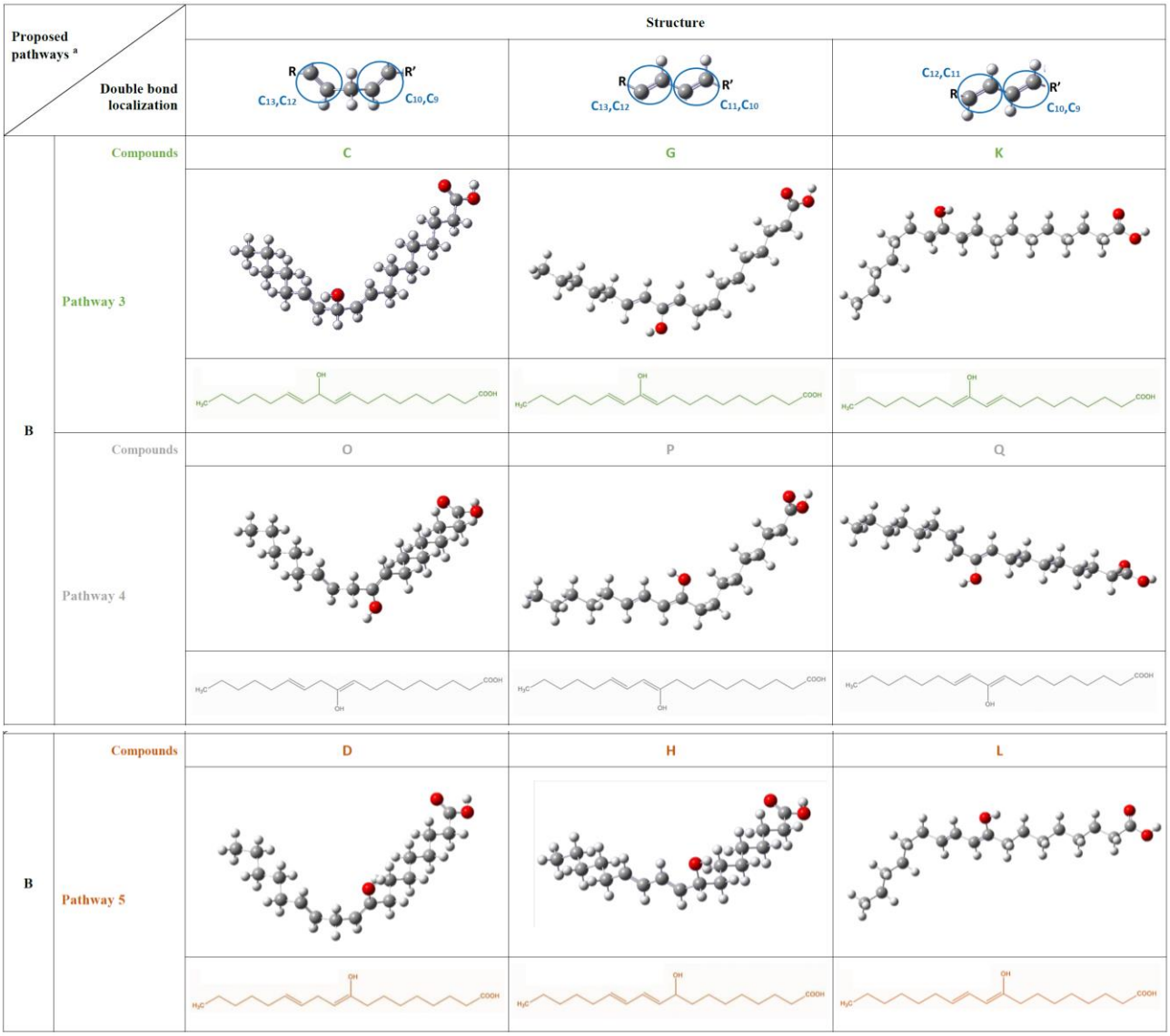

[a] Proposed pathways for the oxidation of linoleic acid (LA). A: Formation of conjugated dienes/trienes. B: Formation of hydroperoxides. Letters A to N denote the proposed final products. Different pathways indicate different oxidation. See Figure 4.

Fig. ESI 2 Optimized structures of linoleic acid (LA) and its proposed oxidation products. Different letters indicate different compounds, and different colors correspond to different routes. Outline colors correspond to the same pattern as that used in Fig. 4.

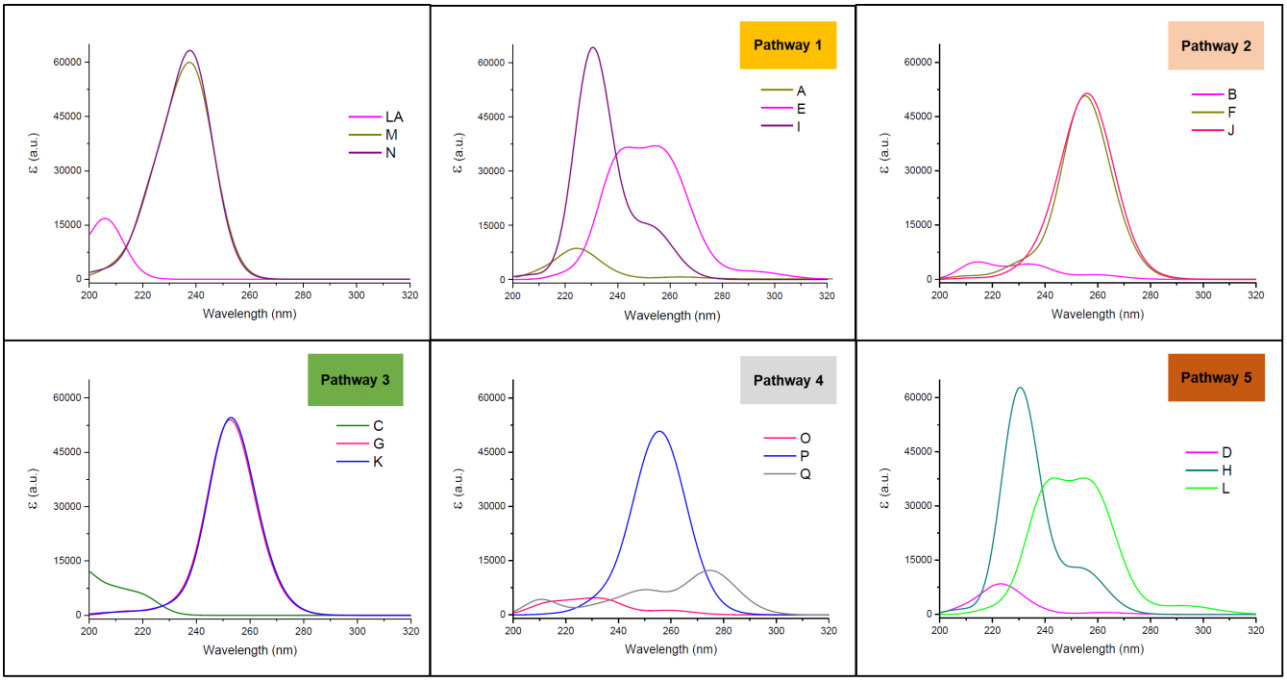

Fig. ESI 3 Theoretical electronic spectra obtained at the DFT(B3LYP) 6-311++G(d,p) level of theory. Each panel corresponds to a different pathway.

Table ESI 1 - Adjustment parameters of the dose-response behavior of the area of the 234 nm band with regard to the exposure time.[a]

Parameter	1 mM H_2O_2	4 mM H_2O_2
A_{min}	0.1797	0.3073
A_{max} (fixed)	7.7	7.7
t_{50} (50% peroxidation) (hours)	2.428 ± 0.028	1.572 ± 0.030
Peroxidation rate (slope) (hours $^{-1}$)	1.228 ± 0.094	3.258 ± 0.221
R^2	0.9982	1

[a] Parameters were obtained by adjusting the experimental data from Fig. 2A, according to Eq. 1:

$$A_{234} = A_{min} + \frac{A_{max} - A_{min}}{1+(10^{(t_{50} - t)n})} \quad \text{Eq. 1}$$

Table ESI 2 Total energy, dipole moments, polarizability, symmetry point groups and rotational constants for dienes/trienes and hydroxy fatty acids proposed as oxidation products, calculated at the B3LYP/6-311++G(d,p) level of theory.

Proposed pathways [a]		Compounds [b]	Total Energy [c] (kJ/mol)	Dipole Moment (Debye)	Polarizability (α) (a.u.)	Symmetry (Point Group)	Rotational constant (MHz)		
							A	B	C
Initial compound		**LA**	-2245915.21	1.38	234.17	C_1	279.63	63.67	52.45
A		**M**	-2245934.86	1.56	246.65	C_1	550.78	45.08	42.28
		N	-2245935.31	1.56	247.15	C_1	1109.95	39.87	39.23
B	**Pathway 1**	**A**	-2443467.06	1.34	237.83	C_1	264.67	62.39	51.58
		E	-2443487.85	2.52	251.98	C_1	496.39	43.43	40.72
		I	-2443468.60	2.12	248.62	C_1	391.69	48.52	43.91
	Pathway 2	**B**	-2443465.50	3.04	238.12	C_1	264.21	62.22	51.45
		F	-2443480.82	2.90	250.69	C_1	558.30	44.22	41.64
		J	-2443489.43	1.72	251.58	C_1	1201.62	38.40	37.95
	Pathway 3	**C**	-2443445.38	2.04	237.93	C_1	250.30	62.70	51.18
		G	-2443481.45	2.02	250.51	C_1	404.05	45.91	41.86
		K	-2443481.77	2.74	250.92	C_1	708.39	40.45	39.14
	Pathway 4	**O**	-2443466.02	2.14	238.29	C_1	243.95	64.44	51.95
		P	-2443489.66	2.02	250.88	C_1	590.22	43.66	41.59
		Q	-2443471.58	2.90	242.55	C_1	748.18	40.40	39.20
	Pathway 5	**D**	-2443466.18	2.91	238.05	C_1	246.11	64.59	52.26
		H	-2443468.51	2.68	247.31	C_1	210.70	68.68	52.85
		L	-2443487.74	3.05	252.42	C_1	839.39	40.08	39.25

[a] Proposed pathways for the oxidation of linoleic acid (LA). A: Formation of conjugated dienes/trienes. B: Formation of hydroxy fatty acids. Letters **A** to **N** denote the proposed final products. Different pathways indicate different oxidation reactions. See Fig. 4.
[b] Compounds are denoted with the same nomenclature as in Fig. 4.
[c] Total energy is the electronic energy, including the zero-point vibrational energy.

Table ESI 3 Predicted vertical excitation energies and associated orbitals transitions major contributions together with oscillator strengths, f, for the dienes/trienes and hydroxy fatty acids proposed as oxidation products, obtained by TD-DFT at the B3LYP/6-311++G(d,p) level of theory after ground-state geometry optimization using the same functional and basis set.

Compounds [b]	$\lambda_{max}^{S_0 \rightarrow S_n}$ **(nm)**	**Oscillator strength f**	**Transition and orbitals major contributions**	
LA	206.76	0.1224	$S_0 \rightarrow S_5$	HOMO->LUMO (12%), HOMO->L+4 (41%), HOMO->L+5 (26%)
M	240.91	0.4687	$S_0 \rightarrow S_1$	HOMO->LUMO (51%), HOMO->L+1 (11%), HOMO->L+3 (13%), HOMO->L+4 (15%)
N	239.76	0.4646	$S_0 \rightarrow S_1$	HOMO->LUMO (47%), HOMO->L+3 (35%)
A	223.32	0.0753	$S_0 \rightarrow S_7$	HOMO->L+6 (17%), HOMO->L+9 (56%)
E	261.58	0.2208	$S_0 \rightarrow S_2$	HOMO->LUMO (11%), HOMO->L+1 (36%), HOMO->L+2 (10%), HOMO->L+5 (30%)
I	229.81	0.3595	$S_0 \rightarrow S_4$	HOMO->LUMO (15%), HOMO->L+1 (39%), HOMO->L+2 (14%), HOMO->L+4 (20%)
B	237.02	0.0389	$S_0 \rightarrow S_2$	HOMO->L+3 (30%), HOMO->L+5 (37%), HOMO->L+6 (22%)
F	253.84	0.6091	$S_0 \rightarrow S_2$	HOMO->LUMO (64%), HOMO->L+2 (16%)
J	259.37	0.4277	$S_0 \rightarrow S_2$	HOMO->LUMO (56%), HOMO->L+5 (27%)
C	209.15	0.0660	$S_0 \rightarrow S_4$	HOMO->L+1 (20%), HOMO->L+3 (28%), HOMO->L+4 (17%), HOMO->L+5 (13%)
G	251.82	0.6810	$S_0 \rightarrow S_2$	HOMO->LUMO (73%), HOMO->L+2 (11%)
K	252.18	0.6924	$S_0 \rightarrow S_2$	HOMO->LUMO (73%), HOMO->L+1 (10%)
O	235.85	0.0405	$S_0 \rightarrow S_2$	HOMO->L+3 (15%), HOMO->L+4 (60%), HOMO->L+5 (10%), HOMO->L+6 (10%)
P	259.99	0.3570	$S_0 \rightarrow S_2$	HOMO->LUMO (51%), HOMO->L+5 (36%)
Q	274.80	0.1676	$S_0 \rightarrow S_1$	HOMO->LUMO (92%)
D	224.52	0.0321	$S_0 \rightarrow S_6$	HOMO->L+1 (16%), HOMO->L+4 (36%), HOMO->L+5 (18%), HOMO->L+7 (12%)
H	229.44	0.4748	$S_0 \rightarrow S_5$	HOMO->LUMO (22%), HOMO->L+1 (10%), HOMO->L+2 (21%), HOMO->L+3 (28%)
L	257.41	0.2965	$S_0 \rightarrow S_4$	HOMO->L+1 (55%), HOMO->L+3 (11%)

[a] Compounds are denoted with the same nomenclature as in Fig. 4