

Flavor & Fragrance Simulation
MMP Flavor/Fragrance Applications
June 2023

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2RM Technology

Molecular Modeling Pro Flavor Plus

1. Physical and Chemical Properties calculated from a molecular odor/flavor and fragrance modeling program
2. Applying these Properties to Develop new flavors/fragrances or to Improve on delivery or cost of existing flavors/fragrances
3. Predicting High impact flavors or aroma
4. Developing time dependent flavor profiles (burst to delay)

Applications

1. Odor and taste thresholds for food and beverage flavors
2. Thresholds for fragrances and environmental volatiles
3. Off-flavor reduction/elimination in food and beverages
4. Provide Cost advantages by optimizing ingredients
5. Currently used in fragrance industry to develop wash off applications candle fragrances and the masking of odors
6. Can be used for designing liquid/semi-solid or solid food flavors

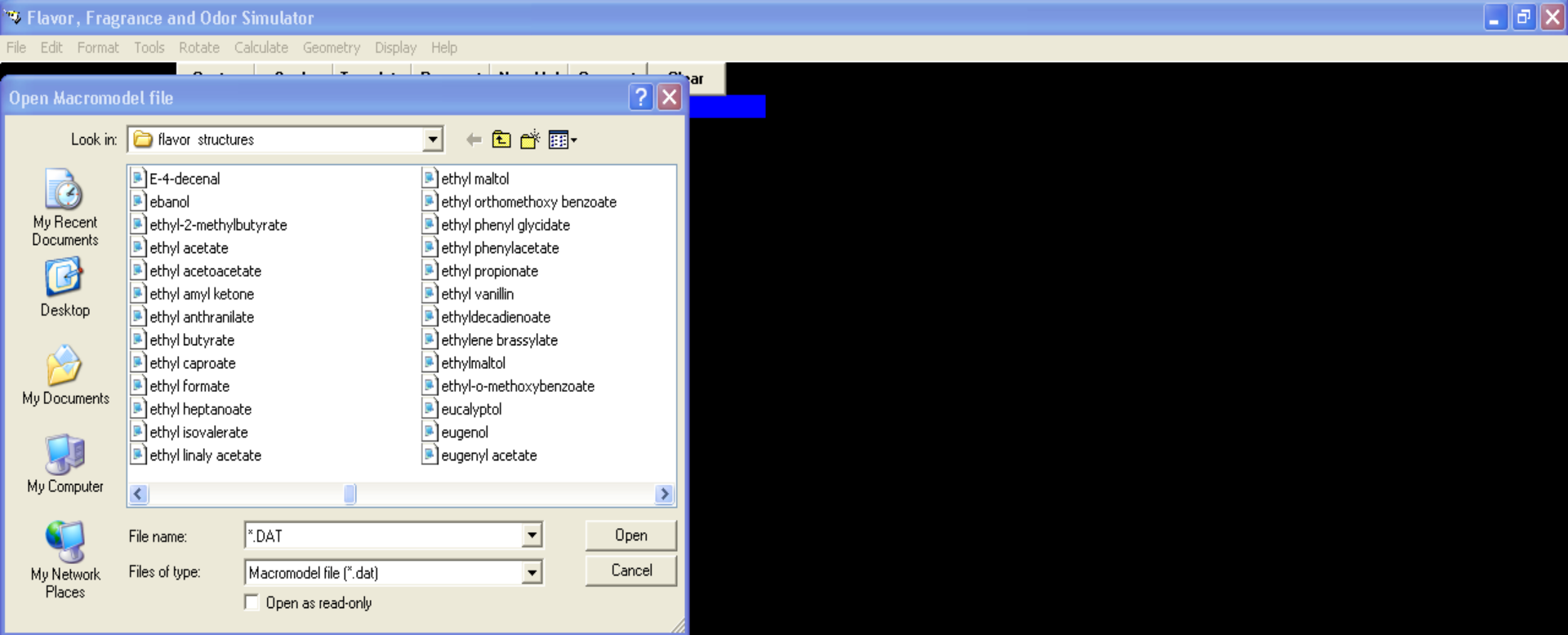
Description of Program

1. A tour of the Flavor & Fragrance Program
2. How to use the information for Flavor Development
3. Example of a Fragrance System and Interpretation
4. Conclusion

Mode is atom addition: Atom = C with bond 1

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-

Initial Screen



Open Database

Center

Scale

Translate

Perspect

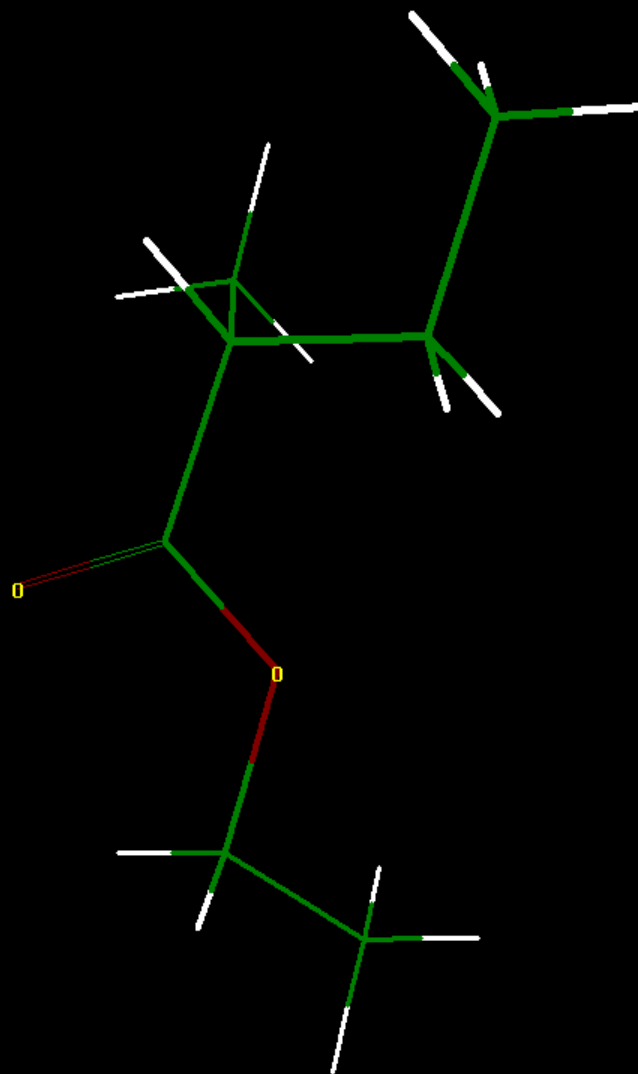
New Mol

Connect

Clear

Mode - Add C with bond 1

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-



Chemical Structure

Center

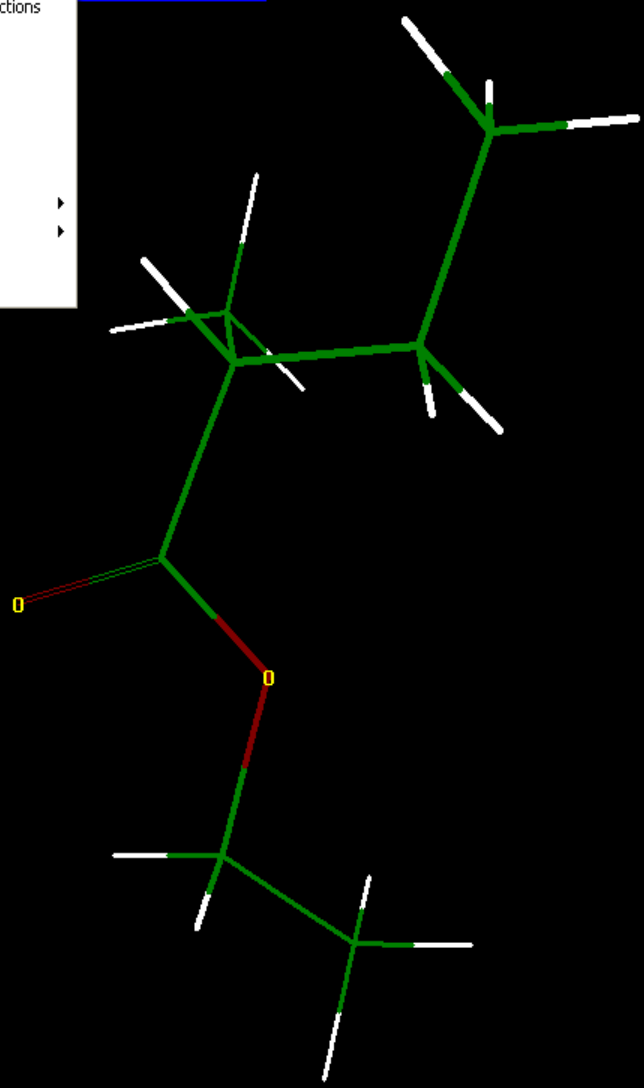
Minimize

Clear

Mode = Add C with bond 1

- Conformational analysis
- Space Molecules Evenly and Show Reactions
- Superimpose and Center
- Dock (compare) molecule on molecule
- Dock molecule with molecule
- Invert
- Mirror
- Identify high strain atom overlaps
- Reference bonds and angles
- Hybridization
- View connection table
- Print Bond Lengths and Angles

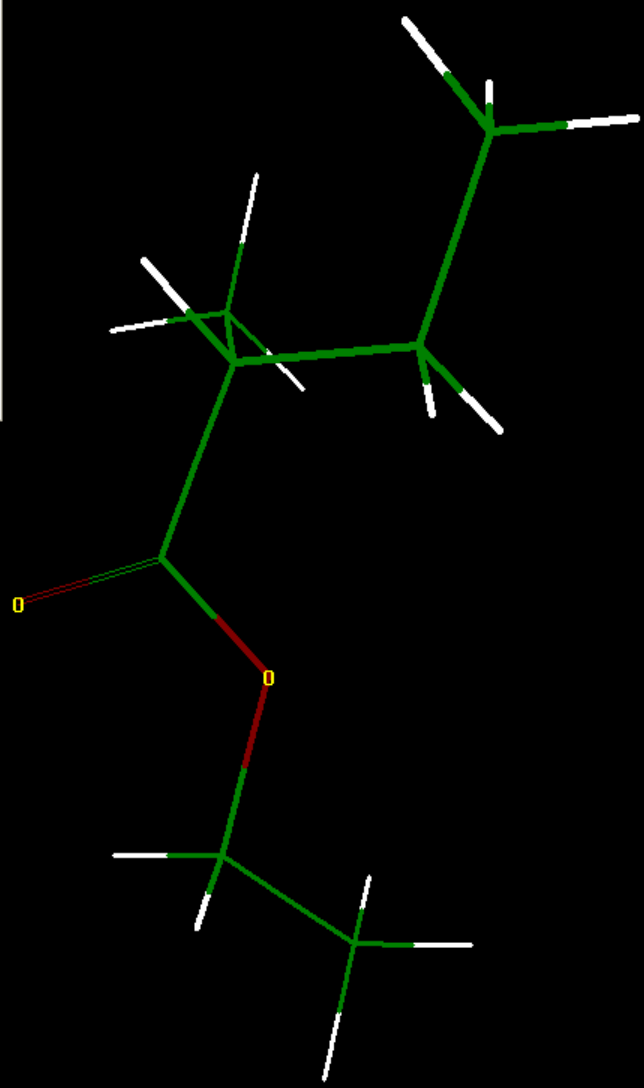
C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-



Open Geometry
& Energy Minimization
(Optional)

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-

- Flavor/Taste and Odor Thresholds
- Inertial Ellipse for Asymmetric centers
- Interatomic Distance
- Angle
- Dihedral Angle
- Current strain
- Molecular weight
- Molecular volume/density
- Dimensions
- Point charges/dipole moment
- Solubility Parameters
- Bioavailability
- Thermodynamics (e.g. boiling pt.)
- Vapor pressure over a range of temperatures
- Mass Percent
- Moments of inertia
- Smiles Notation



Open Calculate
Thresholds

Flavor, Fragrance and ...

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 144.39

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

- water
- acetone
- benzene
- diethyl ether
- ethanol
- ethylmethylbutyrate

Run

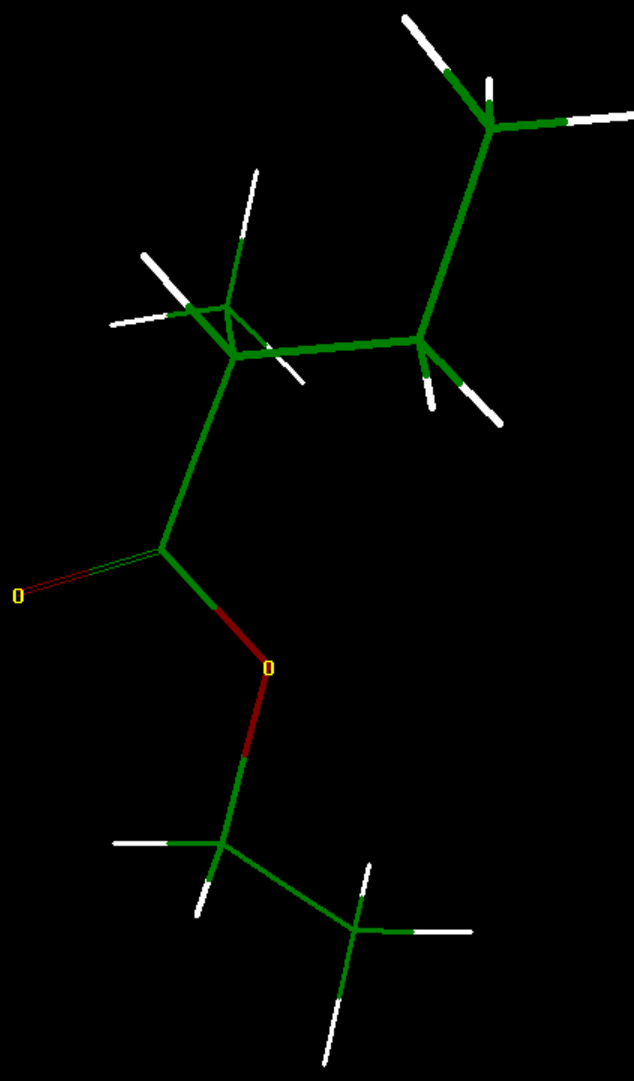
Optional calculation parameters

ppm of the Flavor:

Brix level of beverage:

Density of beverage:

Scale Translate Perspect New Mol Connect Clear



Review Input
BP and Density

Flavor, Fragrance and ...

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 129

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

water

acetone

benzene

diethyl ether

ethanol

ethylmethylbutyrate

Run

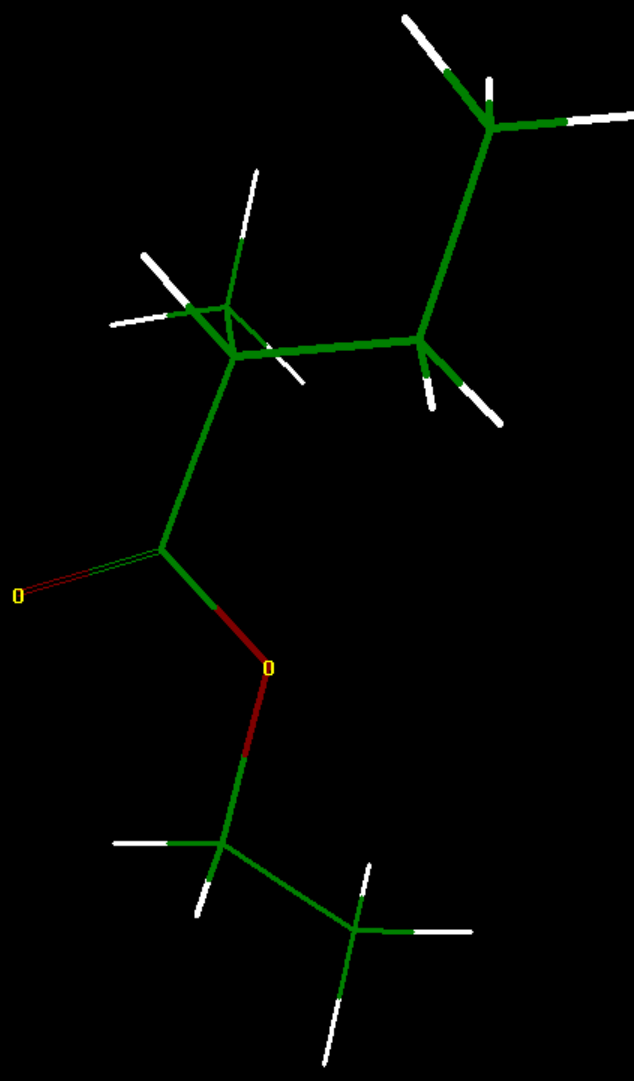
Optional calculation parameters

ppm of the Flavor:

Brix level of beverage:

Density of beverage:

Scale Translate Perspect New Mol Connect Clear



Make Corrections
To BP if needed.
Choose solvent

Flavor, Fragrance and Odor Simulator

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 129

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

water

acetone

benzene

diethyl ether

ethanol

ethylmethylbutyrate

Run

Optional calculation parameters

ppm of the Flavor:

Brix level of beverage:

Density of beverage:

Results (ppm)

Odor threshold: 3.170255E-02 to 9.804741E-02

Taste/Flavor threshold: 0.5520401 to 1.707311

Parameters used in the calculation

Rotational Translational factor (cm sec²): 17.78279

Vapor pressure (atm): 2.555915E-02

Critical compressibility: 0.2654921

Acentric factor: 0.4528425

Second virial component (cm³/mole): -3387.559

Diffusion coefficient (cm² sec): 7.240639E-02

G factor (odor)(cm/sec²): 10171.73

G factor (taste)(cm/sec²): 177121.5

Optional calculation results:

Mole fraction in liquid:

Mole fraction in vapor:

Critical properties

Critical temperature: 573.9105

Critical pressure: 28.03311

Critical volume: 446

Moments of inertia

Component 1: 573.2224

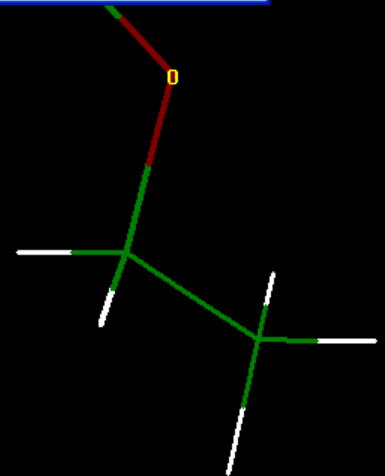
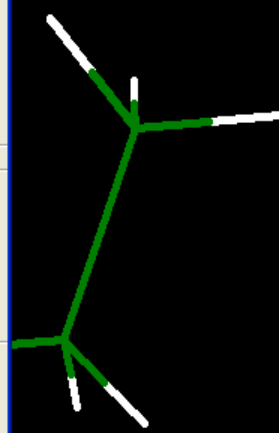
Component 2: 208.0798

Component 3: 643.5346

Radius of Gyration: 3.30826

Print Report

Quit



Run for Initial Calculation of Flavor Properties

Flavor, Fragrance and ...

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 129

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

- water
- acetone
- benzene
- diethyl ether
- ethanol
- ethylmethylbutyrate

Run

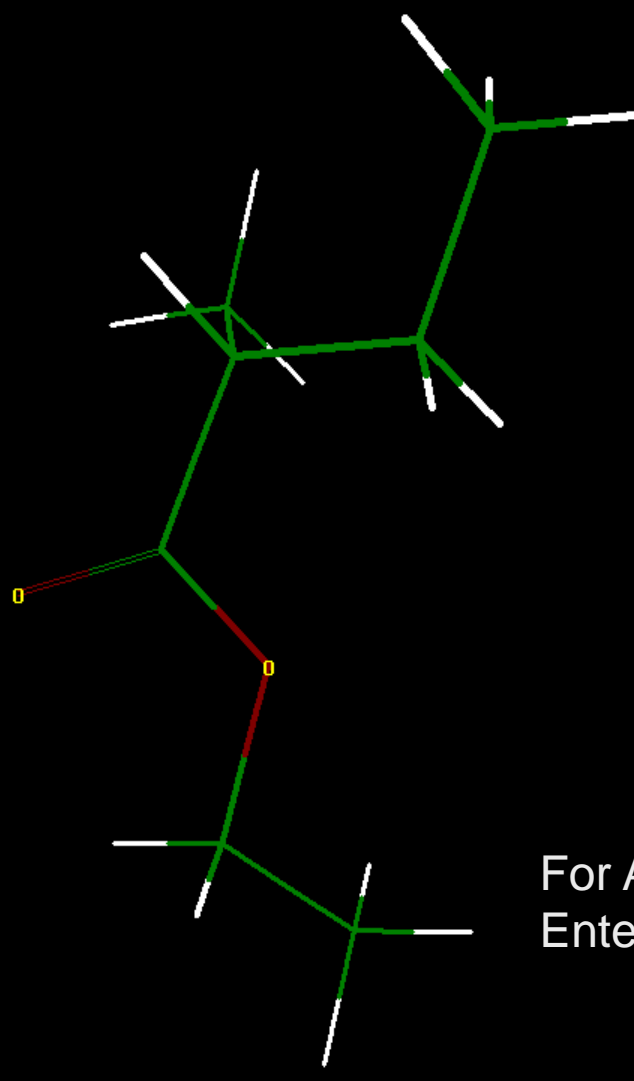
Optional calculation parameters

ppm of the Flavor: 10

Brix level of beverage: 5.0

Density of beverage: 1.09

Scale Translate Perspect New Mol Connect Clear



For Aroma in Water or beverage
Enter optional Parameters

Flavor, Fragrance and Odor Simulator

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 129

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

- water
- acetone
- benzene
- diethyl ether
- ethanol
- ethylmethylbutyrate

Run

Optional calculation parameters

ppm of the Flavor: 10

Brix level of beverage: 5.0

Density of beverage: 1.09

Results (ppm)

Odor threshold: 3.170255E-02 to 9.804741E-02

Taste/Flavor threshold: 0.5520401 to 1.707311

Parameters used in the calculation

Rotational Translational factor (cm sec²): 17.78279

Vapor pressure (atm): 2.555915E-02

Critical compressibility: 0.2654921

Acentric factor: 0.4528425

Second virial component (cm³/mole): -3387.559

Diffusion coefficient (cm² sec): 7.240639E-02

G factor (odor)(cm/sec²): 10171.73

G factor (taste)(cm/sec²): 177121.5

Optional calculation results:

Mole fraction in liquid: 1.333034E-06

Mole fraction in vapor: 1.010146E-03

Critical properties

Critical temperature: 573.9105

Critical pressure: 28.03311

Critical volume: 446

Moments of inertia

Component 1: 573.2224

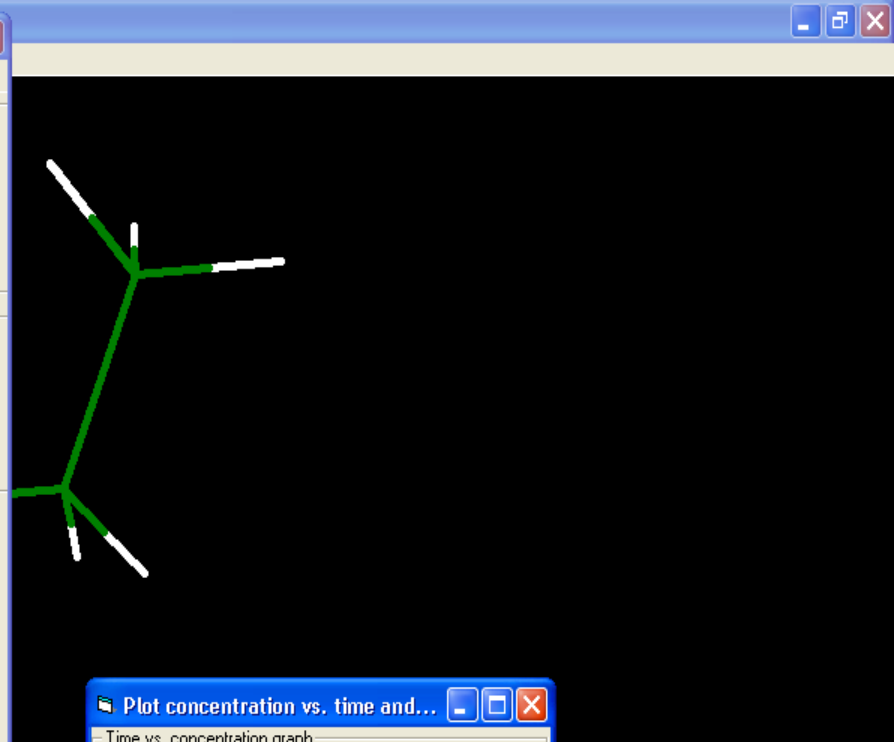
Component 2: 208.0798

Component 3: 643.5346

Radius of Gyration: 3.30826

Print Report

Quit



Plot concentration vs. time and...

Time vs. concentration graph

Maximum time to graph (sec): 600

Distance vs. concentration graph

Maximum distance to graph (cm): 5

Time (sec) for distance vs. concentration: 10

Run **Cancel**

Run Optional Graphs for Vapor Concentrations

The screenshot displays a software interface with several windows. The main window shows a graph titled "Concentration vs. time for ethylmethylbutyrate at 5 cm mg/L flavor in vapor". The y-axis represents concentration in mg/L, with values 0, 0.000003, 0.0326, 0.0555, and 0.0653. The x-axis represents time in seconds, with values 0, 300, and 600. The graph shows a curve that starts at (0,0) and increases, leveling off towards 0.0653 mg/L at 600 seconds. Below the graph, there is a "Density of beverage:" field with the value "1.09".

To the right of the graph is a panel with the following data:

Critical properties	
Critical temperature:	595.8737
Critical pressure:	28.03311
Critical volume:	446
Moments of inertia	
Component 1:	573.2224
Component 2:	208.0798
Component 3:	643.5346
Radius of Gyration:	3.30826

Below this panel are buttons for "Print Report" and "Quit".

A dialog box titled "Flavor and Odor Simulator" is open, asking "Do you want to open the results in an EXCEL worksheet?". It has "Yes" and "No" buttons.

Hand-drawn green lines connect the dialog box to the "Print Report" and "Quit" buttons, and another green line connects it to the graph area.

Ability to Place data in Excel

Flavor, Fragrance and Odor Simulator

Exit Units

User Inputs

Temperature (degrees C): 37

Pressure (atmospheres): 1

Boiling point (degrees C): 144.39

Density: 0.8663743

Molecule name: ethylmethylbutyrate

Choose the solvent:

- water
- acetone
- benzene
- diethyl ether
- ethanol
- ethylmethylbutyrate

Run

Optional calculation parameters

ppm of the Flavor: 10

Brix level of beverage: 5.0

Density of beverage: 1.09

Results (ppm)

Odor threshold: 2.052746E-02 to 6.348587E-02

Taste/Flavor threshold: 0.3443444 to 1.064964

Parameters used in the calculation

Rotational Translational factor (cm sec²): 17.78279

Vapor pressure (atm): 0.0132772

Critical compressibility: 0.2557064

Acentric factor: 0.4528426

Second virial component (cm³/mole): -3946.997

Diffusion coefficient (cm² sec): 7.039453E-02

G factor (odor)(cm/sec²): 6586.213

G factor (taste)(cm/sec²): 110482.5

Optional calculation results:

Mole fraction in liquid: 1.333034E-06

Mole fraction in vapor: 3.912905E-04

Critical properties

Critical temperature: 595.8737

Critical pressure: 28.03311

Critical volume: 446

Moments of inertia

Component 1: 573.2224

Component 2: 208.0798

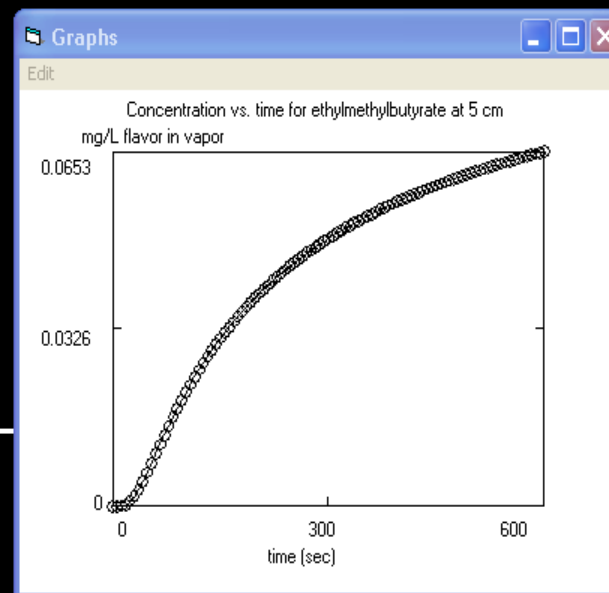
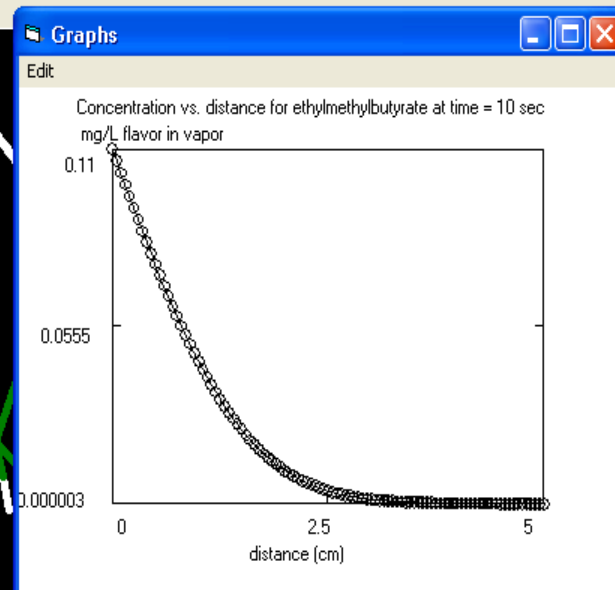
Component 3: 643.5346

Radius of Gyration: 3.30826

Print Report

Quit

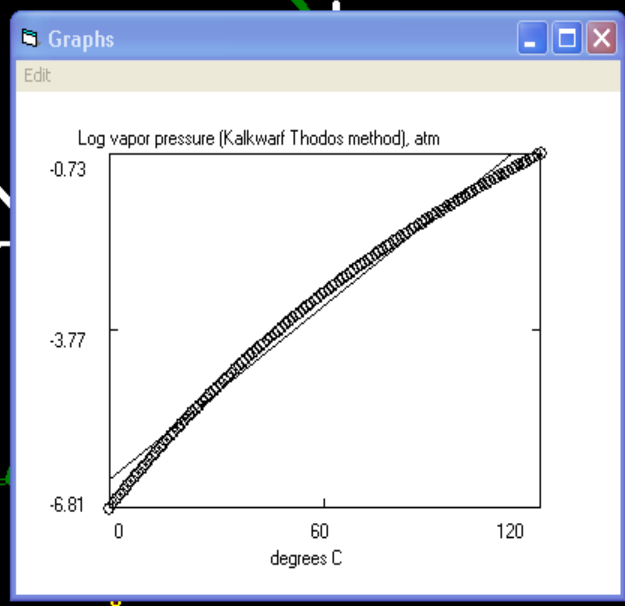
Odor Threshold exceeded at time 10 sec at distance 0 cm. Odor Threshold exceeded at time 102 sec at distance 5 cm.



Air Diffusion and
Concentration Gradients
of compound in
Distance and time

Mode - Add C with bond 1

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-



Statistical output

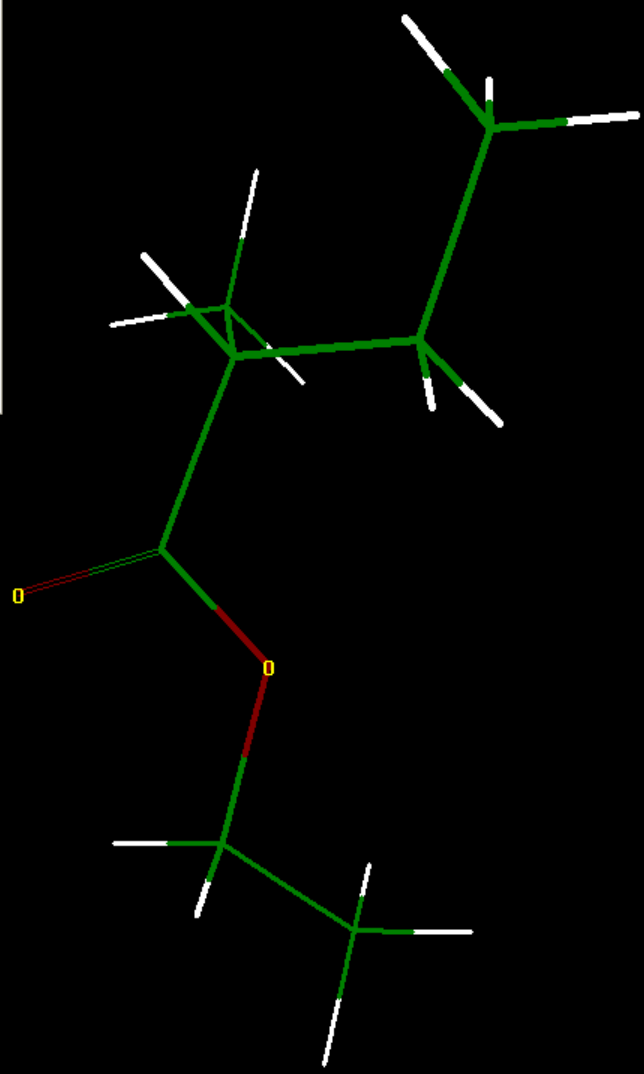
Regression equations for left Y axis:
Log vapor pressure (Kalkwarf Thodos method), atm = -6.316447 + 4.982752E-02*degrees C
r squared= .9866785 n= 121

Ability to Calculate Properties of vapor at Various Temperatures

Mode - Add C with bond

- Flavor/Taste and Odor Thresholds
- Inertial Ellipse for Asymmetric centers
- Interatomic Distance
- Angle
- Dihedral Angle
- Current strain
- Molecular weight
- Molecular volume/density
- Dimensions
- Point charges/dipole moment
- Solubility Parameters
- Bioavailability
- Thermodynamics (e.g. boiling pt.)
- Vapor pressure over a range of temperatures
- Mass Percent
- Moments of inertia
- Smiles Notation

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-



Solubility Predictor

Mode - Add C with bond 1

mmp - Notepad

File Edit Format View Help

```

Solubility Parameters (25 C) for ethylmethylbutyrate:
-- Fragment addition LogP =2.128
-- Atom Based LogP =1.7932
-- Atom Based MR =35.9632
-- Q Log P: N. Bodor and P. Buchwald, J. Phys. Chem. B, 1997, 101: 3404-3412
-- Q Log P= 2.390312
-- Hydrogen bonding number= 2
-- Molecular volume used for QLogP= 119.8848
-- Note: Value of Q Log P will vary slightly from Bodor's due to
      difference in the method of the molecular volume calculation.
-- molecular weight HLB= 2.75809404245717
-- volumetric HLB = 2.77755224993874
-- Hansen's 3-D solubility parameters (delta/sqr(MPa)) -empirical:
-- dispersion = 15.36521
-- polarity = 3.198988
-- hydrogen bonding = 5.918324
-- solubility parameter = 16.77348
-- van Krevelen and Hoftyzer's 3-D solubility parameters (JA(1/2))/(cm^(3/2))):
-- dispersion = 15.57508
-- polarity = 3.261449
-- hydrogen bonding = 6.825842
-- molar volume (cm^3/mol) = 150.24
-- solubility parameter = 17.31509
-- Note: some references use cal^(1/2)/cm^(3/2) [divide above by 2.046 to convert].
-- Hoy's system (1985) for calculation of the 3-D solubility parameters ((JA(1/2))/(cm^(3/2
))) :
-- molar attraction function (solubility parameter) = 19.70002
-- dispersion = 14.62914
-- polarity = 7.491348
-- hydrogen bonding = 10.86089
-- molecular aggregation number= 1.436671
-- Energy of cohesion (J/mol)(Ref: Hoy)= 39748.55
-- molar volume = 129.01
-- Energy of cohesion (J/mol)(Ref: Fedors)= 45440
-- hydration number =1.5
-- hydrophilic surface area = 2.19178273018375 cm^2/mol x10^9
-- % hydrophilic surface area = 18.3395393150312

```

C	N
O	H
P	S
F	Cl
Br	I
Other	
Rings	
Add	
Change	
Delete	
0	1
2	3
+	-

Definition Aroma -

- Optimal release of flavor compound based on releasing media and physico-chemical properties of the flavor.
- These properties can be measured experimentally, defined empirically or calculated using physical properties.
- Define “Aroma” or “optimized release values” as the value of a calculated **release pressure** of a flavor out of water (or a chosen specific food or solution) per time.
- Water release pressure is the product of the diffusion coefficient X G factor (odor) X odor threshold (ppm)

Predictive Importance of Aroma Release Values

- Release accurately predicts the release order in time of materials in a multi-flavor system
- Release can be calculated for any flavor/fragrance. Multiply release by parts added and order from highest to lowest.
- Ability to group materials in release order to further control aroma hedonics and engineer consumer perception.
- Ability to design new flavors and hedonics

Example For a System of Flavors/Fragrances Predicting the Aroma on Dilution with Water

Calculation of total release pressure, and
Impact on release using 50 flavor/fragrance components

The following slides show odor predictions:

1. Order of release of 50 components from a mixture at a given composition based on order of magnitude changes in release pressure
2. The order is of undefined time but usually represents 5 second intervals
3. Within each order is a major impact component
4. Odor impact calculation for each component can be determined by running optional graphs of vapor concentration and comparing concentration in vapor with respect to odor threshold.

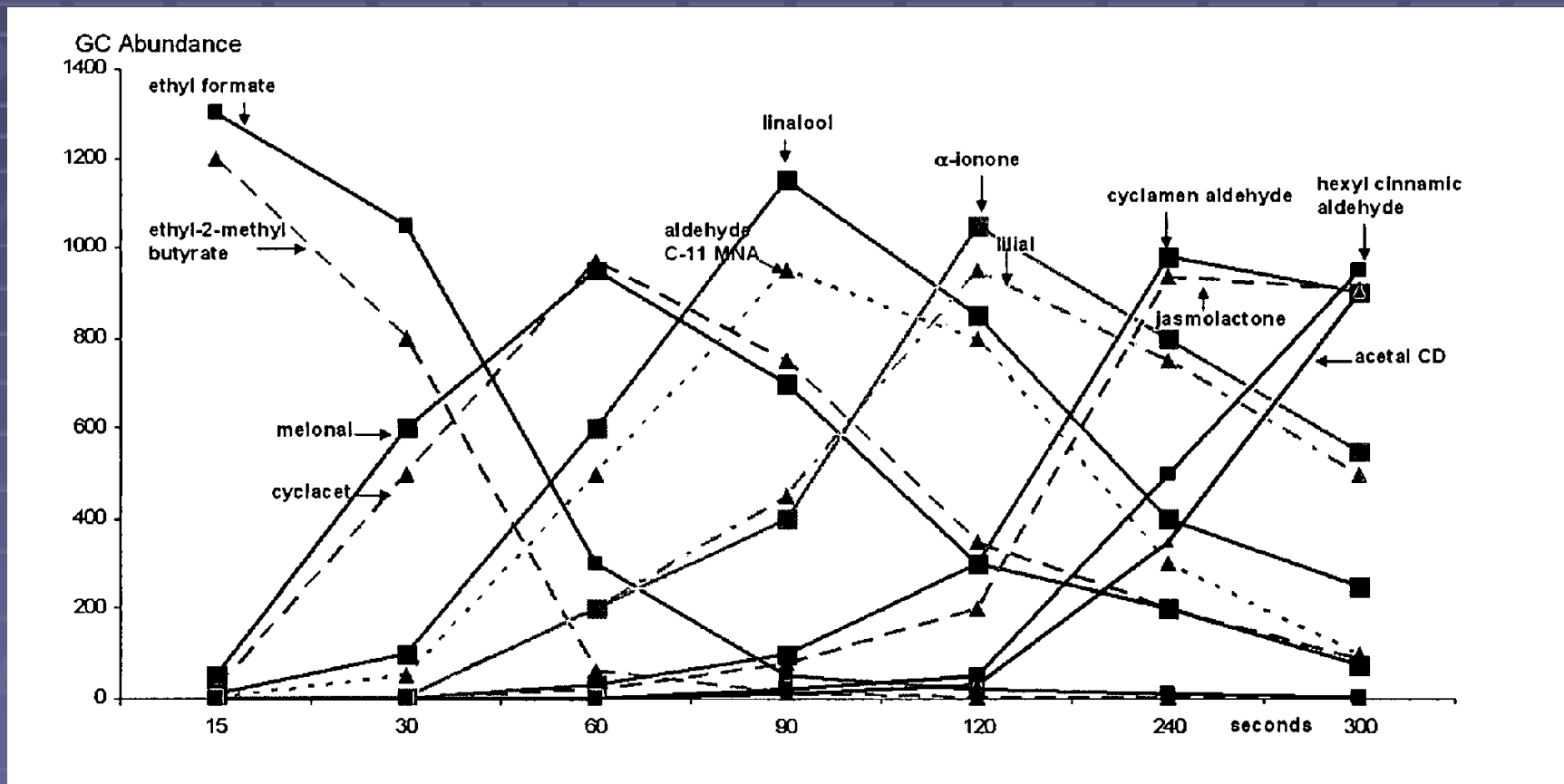
Example Calculation of Release and Total Release
 And Ordering of 50 Fragrances in Order of release:
 Colors represent magnitude change in total release
 Initial release 0 seconds to 20 seconds

	<u>parts</u>	<u>clogP</u>	<u>B.P.</u>	<u>Water Release Value Ω</u>	<u>$\Omega \times Qty$</u>	<u>%</u>	<u>$\Omega \times \%$</u>
d-LIMONENE	2	4.83	174.00	12.89011949473	25.780238989	0.023781213	0.306542675
ETHYL BUTYRATE	0.1	1.77	121.95	70.55231284335	7.055231284	0.001189061	0.083890978
ETHYL 2-METHYLBUTYRATE PUR	0.1	2.26	129.00	55.94787687423	5.594787687	0.001189061	0.066525418
MANZANATE	0.1	2.76	156.32	5.90364669599	0.590364670	0.001189061	0.007019794
LII	9	3.28	198.50	0.03077016006	0.276931440	0.107015458	0.003292883
DI	3	3.60	192.00	0.06353152707	0.190594581	0.035671819	0.002266285
TF	0.3	2.67	189.16	0.33000000000	0.099000000	0.003567182	0.001177170
RI	0.1	3.13	196.74	0.58404016932	0.058404017	0.001189061	0.000694459
CI	0.2	1.61	156.00	0.25661199021	0.051322398	0.002378121	0.000610254
EI	1.3	2.08	216.00	0.03934973997	0.051154662	0.015457788	0.000608260
CI	0.7	3.56	225.00	0.05793558671	0.040554911	0.008323424	0.000482222
VE	2.5	4.42	239.00	0.00971745877	0.024293647	0.029726516	0.000288866
AL	0.5	3.67	210.00	0.04323356349	0.021616782	0.005945303	0.000257037
AL	0.5	2.08	214.00	0.04188905618	0.020944528	0.005945303	0.000249043
CI	0.1	2.61	198.00	0.18024312711	0.018024313	0.001189061	0.000214320
ET	2.9	3.87	220.00	0.00418909839	0.012148385	0.034482759	0.000144452
EI	0.5	2.57	222.00	0.02298313800	0.011491569	0.005945303	0.000136642
FRUCTONE	0.3	1.30	207.99	0.03465057668	0.010395173	0.003567182	0.000123605
LIF	0.1	2.48	184.78	0.10283040388	0.010283040	0.001189061	0.000122272
DIH'	0.2	3.10	201.00	0.03596706525	0.007193413	0.002378121	0.000085534
IONONE BETA PURE	0.9	3.96	239.00	0.00733636218	0.006602726	0.010701546	0.000078510
DII,	1	3.44	250.00	0.00445927024	0.004459270	0.011890606	0.000053023
VEI	0.1	4.42	237.00	0.01121131905	0.001121132	0.001189061	0.000013331
TEI	0.1	4.34	239.87	0.01009611655	0.001009612	0.001189061	0.000012005

Continued Release values of 50 Fragrances at 20 and 25 seconds

		<u>parts</u>	<u>clogP</u>	<u>B.P.</u>	<u>Water Release Value Ω</u>	<u>Ω x Qty</u>	<u>%</u>	<u>Ω x %</u>
FL		2.5	1.65	243.05	0.00018830080	0.000470752	0.029726516	0.000005598
TE		0.1	3.33	218.00	0.00450287663	0.000450288	0.001189061	0.000005354
CO)		0.01	2.31	226.46	0.03278790317	0.000327879	0.000118906	0.000003899
UM		0.6	3.90	238.50	0.00052269564	0.000313617	0.007134364	0.000003729
FL		0.3	3.91	260.00	0.00099601267	0.000298804	0.003567182	0.000003553
AL	PROPIONAT	0.3	4.12	265.27	0.00094605475	0.000283816	0.003567182	0.000003375
HE	EHYDE	15	4.90	308.70	0.00001630285	0.000244543	0.178359096	0.000002908
GF	NE	0.3	2.38	266.88	0.00058484054	0.000175452	0.003567182	0.000002086
GAMMA UNDECALACTONE		0.3	3.06	260.00	0.00047556253	0.000142669	0.003567182	0.000001696
alpha-DAMASCONE		0.1	3.62	260.00	0.00136091601	0.000136092	0.001189061	0.000001618
MAC	719	3	2.83	296.58	0.00004273000	0.000128190	0.035671819	0.000001524
HEL		1.4	2.51	286.03	0.00002808947	0.000039325	0.016646849	0.000000468
ADC		0.4	5.35	286.90	0.00008031443	0.000032126	0.004756243	0.000000382
BEN		0.2	1.08	205.40	0.00015965114	0.000031930	0.002378121	0.000000380
BAC		1.5	5.14	276.69	0.00002111182	0.000031668	0.017835910	0.000000377
GAL	I	10	6.06	345.00	0.00000288325	0.000028832	0.118906064	0.000000343
HEI		15	2.90	307.00	0.00000139777	0.000020967	0.178359096	0.000000249
SAN		1.3	5.15	275.79	0.00001362896	0.000017718	0.015457788	0.000000211
DAMASCENONE		0.03	4.04	275.64	0.00049168874	0.000014751	0.000356718	0.000000175
C/		0.03	2.43	266.07	0.00019327221	0.000005798	0.000356718	0.000000069
AM		0.03	4.76	345.00	0.00004104660	0.000001231	0.000356718	0.000000015
ET	SYLATE	4.3	4.71	333.00	0.00000028348	0.000001219	0.051129608	0.000000014
CO)	ALS	0.4	1.48	292.20	0.00000261059	0.000001044	0.004756243	0.000000012
VE	l	0.1	5.36	340.00	0.00000452415	0.000000452	0.001189061	0.000000005
E)	AL	0.2	6.15	344.80	0.00000149013	0.000000298	0.002378121	0.000000004
ME	E	0.1	2.84	319.79	0.00000000324	0.000000000	0.001189061	0.000000000

Graph of Odorant Residence Time in Headspace According to their Release Values



Reference: Perfumes for Rinse-Off Systems U.S. Patent 7,446,079 B2

Odor Evaluation of 50 component mixture and Hedonic Progression from Water

Water Release Order Predicts

Citrus tangerine

Green floral apple

Floral

Peach tropical, papaya

Floral musk

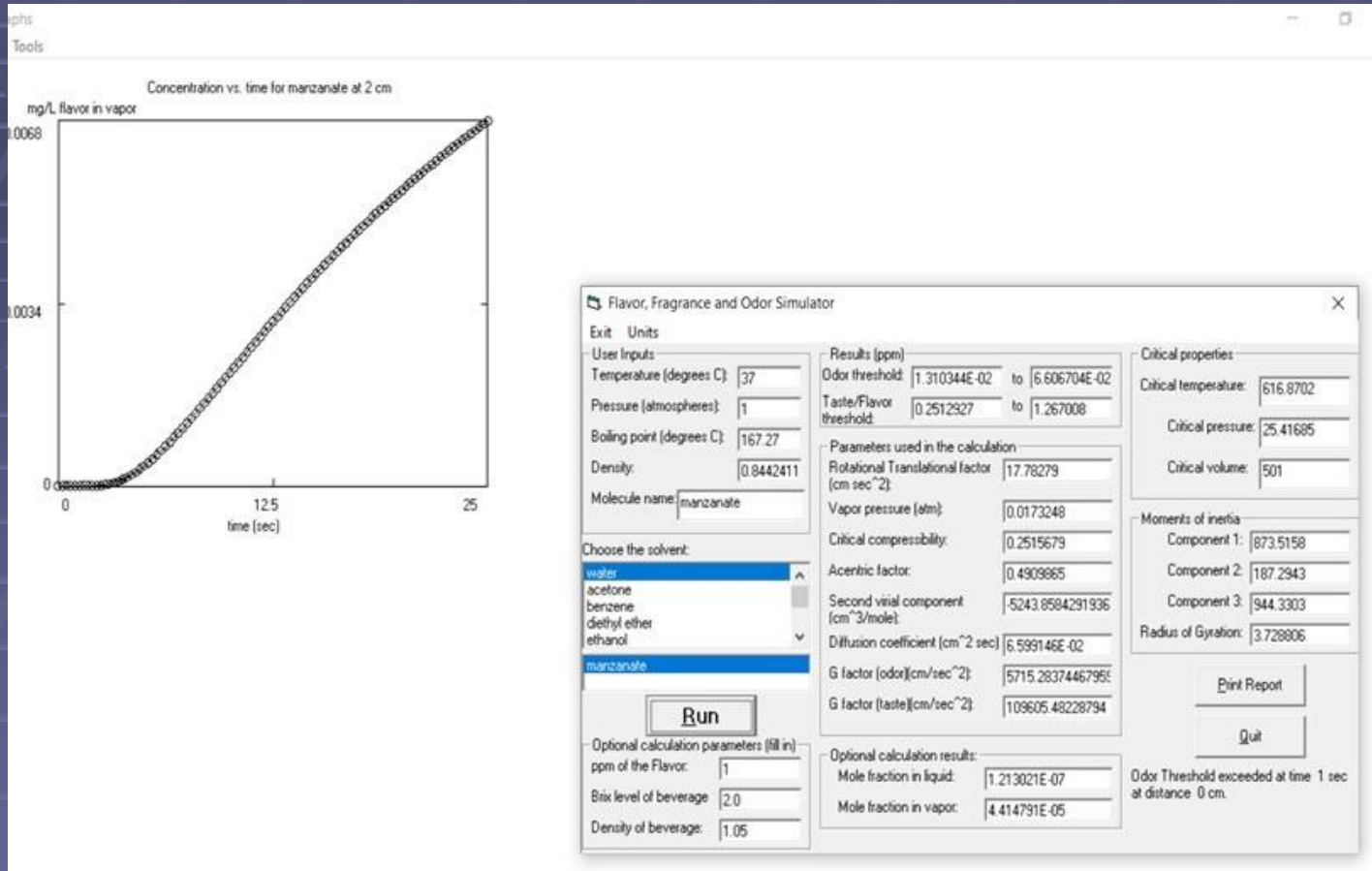
Evaluation Comments:

“A lot of pop, tropical fruity citrus, grapefruit citrus blend, green, cassis, floral amber” -

“Cucumber floral aldehydic, apple, rose”

“Floral, fresh citrus grapefruit orange, musk, floral peach woody”

Predicting Odor Impact within a Release Group



Compare Concentrations in Headspace at 25 seconds with Odor Threshold to Calculate an Odor Index ($0.0068/0.0131 = 0.519$)

Rationale for Flavor Design

- Values for total water release are quantity related:

$$\text{Release}_{\text{final}} = (\text{parts in formula}) \times \text{Release}$$

- Able to move up and/or down the defined “release” depending on the **composition** in formula and value of Release: dynamic and flexible design of flavors within a specific formula
- Able to predict residence time or duration of aroma by overdosing on **specific release or compounds within certain release group**
- **Better control of aroma profile and ability to focus on the hedonic fingerprint of certain release times by engineering the previous and/or targeted ones** – I.e. burst or fresh release perception of certain notes or change of hedonic impression of the released flavor after a certain time

Computer Applications in Flavor/Fragrance Design

Capabilities for Criteria for Success:

- Optimize aroma or water release formulations using predicted properties
- Engineer flavor aroma character according to calculated release profiles
 - Cost considerations and economical advantages can be predicted
 - Predict odor indices related to ODT in air and in liquid
 - Program can be applied to water/emulsion systems, flavor burst, and with off-flavors or other systems requiring flavor modeling

See-US Patent 7446079B2 for more details