DESIGN OF SUSTAINABLE REFRIGERANTS BY MULTI-SCALE MODELING

Abstract

As Europe enforces mandates to substantially phase down the emission of high global warming potential refrigerants, a pressing challenge emerges in the refrigeration and air conditioning industry: the **development of environmentally sustainable alternatives to hydrofluorocarbons**. In response, this contribution focuses on the **implementation of multiscale modelling tools for the development of a consistent methodology to identify new refrigerants with lower emissions**. The proposed approach relies on the robust **polar soft-SAFT** equation of state to **predict thermodynamic properties** required for their technical evaluation at conditions relevant for cooling applications, in combination with **artificial intelligence neural networks integrated using molecular descriptors through COSMO-RS**. Overall, the strength of this methodology lies in the development of accurate coarse-grain models that provide the required data for the rational design of new refrigerants, without the need of further experiments. Based on these data, an **energy, exergy, economic and environmental (4E) analysis** is conducted to minimize retrofitting costs of existing systems, in order to address data gaps and enhance the accuracy of predictions for thermodynamic properties and system performance. This framework is applied across a wide range of operating conditions and system configurations to ensure robustness and accuracy in the context of waste-heat recovery, **finding a potential blend [(60/40) *wt.*% R1243zf + R1234ze(E)] that can effectively replace R134a**. A multi-objective optimization method using statistical tools has been developed to assess the impact of design factors on potential enhancements in cooling cycle performance, finding annual cost savings and reduction in CO_2 emissions. Additional analysis of environmental impact and projected cost is included to quantify the impact associated with their use and emissions, aiding in the identification of appropriate drop-ins from a holistic techno-environmental-economic perspective. Further **studies on lubricant leaks and their impact on cycle efficiency** have revealed minimal effects, with the balance between solubility, miscibility, and viscosity as of main concern. Finally, this thesis explores promising **retrofitting alternatives to CO_2**, overcoming its safety limitation in sub-critical cascade cycles, extending the methodology presented to non-fluorinated compounds. Overall, the results indicate the capability of the approach, based on molecular modelling tools in providing an adequate framework to address the challenge of reducing emissions in the refrigeration industry, following guidelines by the European Commission.

Problem Statement and Current State of the Art

The persistent effects of global warming have consistently increased average global surface temperatures, recording a 1.36 °C above the 20th century average as of date, predicting the year 2024 to be the warmest on record [1]. In face of these warming trends, the global population has increased its demand for domestic and industrial space cooling to counter act the increasing temperatures and extreme heat waves. As of 2022, approximately 2 billion air-conditioning (AC) units are in operation worldwide, mainly owned by 37% of global population, and projected to nearly double by 2050, with expected growth in population, income and living standards, and more importantly, global raising temperatures

[2,3]. By 2050, nearly 75% of global households will own an AC unit, with leading economies in developing countries including India, Indonesia, and People's Republic of China accounting for 50% of total owned AC units.

The associated energy consumption for AC units is absent from the energy debate, though accounting for nearly 20% of total building electricity consumption, marking 10% of global electricity use [2,3]. This is a rapidly growing energy consumption segment, increasing by nearly 5% annually, and expected to reach 40% of global electricity usage by 2030, and triple by 2050, making space cooling the fastest growing energy use in buildings and one of the top drivers for global electricity utilization. This might impact peak electricity demand, leading to more frequent power outages, especially during hot seasons, requiring additional power plants to meet required electricity demand [4]. Even though electricity production is shifting towards low-carbon resources such as natural gas, renewable energy, and others, still, indirect CO_2 emissions from space cooling are growing, reaching 1 gigatons (Gt) in 2022, and projected to triple by 2050, further aggravating the increasing warming trends [2–5].

To deal with this phenomena, refrigeration and air conditioning technologies have experienced a transformative evolution [6], driven primarily by the changing landscape of fluorinated gases (F-gases), a subgroup of greenhouse gases (GHGs) primarily used for cooling applications. Investing in more efficient ACs is another key factor in developing sustainable cooling infrastructure; hence, the energy efficiency of the cooling cycle can be directly enhanced through either optimization of operating conditions, deployment of novel fluids, or cycle configurations and designs.

The evolution of refrigerants traces a path through various generations [7], leading to the adoption of simple yet functional compounds like water, ammonia, carbon dioxide, and methyl chloride (CH_3Cl) in early applications. Initially revolutionary [8], these first-generation refrigerants were eventually replaced due to safety concerns including ammonia's high toxicity, carbon dioxide's high pressure requirements, and CH_3Cl's flammable and toxic nature. This quest for safer alternatives [9] paved the way for the development of next generation of refrigerants [10,11], transitioning from chlorofluorocarbons (CFCs) as with Freon (R12) in the 1930s, valued for non-flammability, to hydrochlorofluorocarbons (HCFCs) such as R22 in the 1980s, with lesser ozone impact but still highly pollutant, and finally to hydrofluorocarbons (HFCs) as with 1,1,1,2-tetrafluoroethane (R134a) in the 1990s, which, while ozone-safe, is currently targeted due to high-global warming potential (GWP) standards. In this manner, and according to the latest report from the National Oceanic and Atmospheric Administration (NOAA), although atmospheric levels of HFCs are significantly lower compared to CO_2, (*i.e.,* 237 ppt for HFCs *vs.* 410 ppm for CO_2) [12], the substantial emissions of these have undeniably impacted the average surface temperature, outpacing the long-term average trend from 1901 up to date.

Each stage of this evolution, defined by distinct environmental impacts and regulatory measures [13], has propelled the advancement of sustainable cooling technologies, furthering global initiatives to adopt more environmentally friendly solutions. This transition to a new generation of refrigerants, along with global long-term initiatives, is outlined in **Figure 1**, summarizing the main collective global goals in the fight against climate change, primarily driven by the introduction and later approval of the 2016 Kigali Amendment [14] on the original Montreal protocol. As of September 2024, the Kigali Amendment has been ratified by 160 countries, representing approximately 88% of the global population and accounting for 98% of global HFCs consumption. Among these, top HFC-producing nations—China, the United States, India, the European Union, and Japan—all ratified the Kigali

Amendment no sooner than 2021, with the exceptions of the EU and Japan. In addition to Kigali's environmental protection agreement, regional and national regulations have also emerged as competent legal basis to attend the environmental drawback related to HFCs disproportioned emissions. European directive 2006/40/EC [15] came into effect on January 2017 and is consistent with the steady replacement of R134a (GWP=1360) in new air conditioning vehicles equipment, while (EU) legislation No 517/2014 [16] states a manufacture and consumption total veto on HFCs with a GWP greater than 2500 since the beginning of 2020, reducing up to 150 by 2022. This is projected to target a 80 – 95% reduction of HFCs emissions by 2050 [17,18], with a recent proposal for an even more ambitious phase-down, thus aligning with the European Green Deal and the European Climate Law. This would lead to a consumption reduction of 102.5 megatons of CO_2 equivalent by 2030, with a further annual decrease of 20.1 Mt thereafter. Nationwide legislation in the U.S. has both incentivized the production of low-GWP refrigerants and restricted the usage of 3rd generation commercial coolers. Building on these efforts, the American Innovation and Manufacturing (AIM) Act, enacted in late 2020, sets ambitious targets to reduce HFC production and consumption by 85% by 2036, significantly addressing their contribution to global warming.

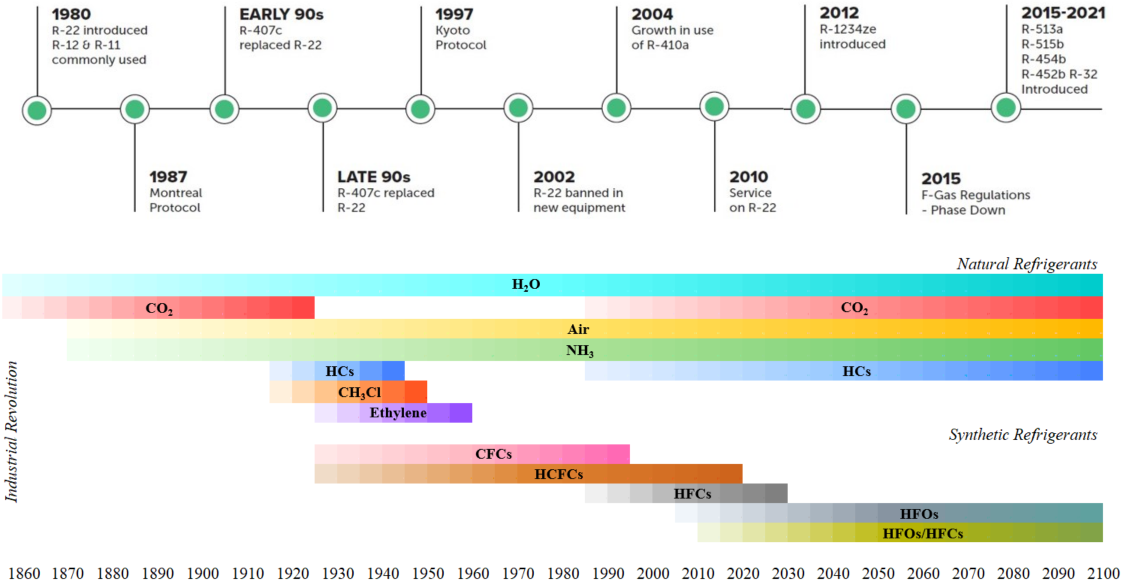

Figure 1. *Evolution of refrigerants by family from the industrial revolution to the present, with projections into the 22nd century and enacted regulations over time.*

Seeing that the complete removal of HFCs from market circulation is imminently close, it is necessary to find an answer to the question *"what are the alternative sustainable refrigerants replacing the technically efficient HFCs?"*. The National Institute of Standards and Technology (NIST) developed a framework to investigate new classes of potential refrigerants meeting imposed environmental and safety regulations, while maintaining the technical efficiencies of widely used high-GWP HFCs [19].

From a pool of 56000 single-component refrigerants, limited options for low GWP refrigerants arise, with merely **27 potential candidates balancing environmental, safety, and technical trade-offs, mainly from hydrofluoroolefins (HFOs)** [20], commonly called 4th generation refrigerants. Additional investigations on the operational compatibility of pure HFOs and hydrochlorofluoroolefins (HCFOs) as drop-in replacements (*i.e.,* having the capacity to substitute current HFCs to existing systems with minimal modifications) identified their potential to only replace a small pool of commercial single-component HFCs (*e.g.,* R134a, 1,1-difluoroethane (R152a), and 1,1,1,3,3-pentafluoropropane (R245fa)), with no viable replacements for the majority of widely used HFCs [21]. Though several low GWP refrigerants have been recently identified [8,17,22,23], their market deployment is constrained by several barriers in global and country-specific contexts, spanning across (1) technical barriers of safety-related properties and limited range of applications, (2) technological barriers related to high investment costs either for retrofitting existing systems or deploying newly designed systems with low GWP refrigerants, and (3) commercial barriers associated with misaligned commercial interests of industrial sectors with imposed regulations.

To overcome this limitation, a more effective approach involves **designing refrigerant blends that can circumvent existing barriers towards deployment of low GWP refrigerants, based on robust thermodynamic models**. A summary of promising replacements that are ready for commercialization based on GWP < 600 listed in **Table 1**. While zeotropic blends can lead to operational issues, the market's limited supply of fully azeotropic blends (only 17 mixtures registered and classified in the R500 series)—many of which have high ODP or GWP—makes near-azeotropic alternatives, an increasingly preferred choice. Their use is well-established, as demonstrated by the introduction of R410A, a (50/50) *wt.*% blend of difluoromethane (R32) and pentafluoroethane (R125), during the phase-out of chlorodifluoromethane and dichlorodifluoromethane [24,25]. Similarly, synthetic medium-GWP blends (i.e., GWP ≈ 500–750) exploiting low-GWP HFOs and non-flammable HFCs such as R513A and R450A, have been proposed as mid-term drop-ins for R134a, given their high technical performance [26,27]. However, **their adequacy must be re-evaluated with the realigned GWP constraints, hence, the need for alternative ultra-low-GWP (<150) synthetic blends**.

Table 1. *Summary of alternative drop-in replacement blends, specifying their proportion, GWP, ASHRAE safety classification, normal boiling point (NBP) and glide temperature (T_G).*

Blend	*wt.%*	GWP	ASHRAE	*NBP* / °C	T_G / K	Baseline	Ref.
R1234ze(E) + R152a	10/90	112.2	A2	-24.41	0.013	R134a/R410A	[28,29]
R600a + R1234ze(Z)	90/10	18.6	A3	-11.77	0.001	R134a/R410A	[28]
R600a + R1233zd(E)	90/10	31.4	A3	-11.92	0.031	R134a/R410A	[28]
R450A (R1234ze(E) + R134a)	58/42	547	A1	-23.36	0.640	R134a	[28,30–32]
R513A (R1234yf + R134a)	56/44	573	A1	-29.58	0.000	R134a	[30]
R1234ze + R134a	90/10	150	A2L	-21.40	0.930	R134a	[33,34]
R430A (R152a + R600a)	76/24	107	A3	-27.60	0.200	R134a	[35]
R431A (R290 + R152a)	71/29	43	A3	-43.20	0.000	R134a	[35]
R435A (RE170 +R152a)	80/20	30	A3	-26.00	0.200	R134a	[35]
R436A (R290 + R600a)	56/44	<3	A3	-34.30	8.200	R134a	[35]
R600a + R1224yd(Z)	90/10	18.1	A2L – A3	-12.03	0.081	R134a/R410A	[28]
R1243zf + R152a	10/90	111.7	A2	-24.88	0.103	R134a/R410A	[28]
R600a + R236ea	90/10	138	A2L – A3	-12.18	0.217	R134a/R410A	[28]
R1234yf + R152a	10/90	112	A2L – A2	-25.13	0.236	R134a/R410A	[28,34]
R600a + R245fa	90/10	121	A3	-12.97	0.756	R134a/R410A	[28]
R152a + R600	90/10	99.8	A2	-25.92	0.194	R134a/R410A	[28]
R454A (R32 + R1234yf)	35/65	238	A2L	-47.80	5.000	R404A	[36,37]
R454C (R32 + R1234yf)	21.5/78.5	146	A2L	-45.50	6.000	R404A	[36–38]
R32 + R1234yf + R744	22/72/6	149	A2L	-57.50	14.120	R410A	[39]
R455A (R744 + R32 +R1234yf)	3/21.5/75.5	146	A2L	-52.00	9.860	R404A	[37,38]
R457A (R32 + R1234yf + R152a)	18/70/12	139	A2L	-42.60	6.140	R404A	[38]
R459B (R32 +R1234yf +R1234ze(E))	21/69/10	143	A2L	-45.00	7.040	R404A	[38]

R600 (*n*-butane), R600a (*i*-butane), R774 (CO_2) and RE170 (Dimethyl ether).

Outcomes, Implementation, Innovation and Applications

The PhD thesis has been devoted to **developing a comprehensive methodology, encompassing multiple simulation tools, to identify effective 4th generation drop-in refrigerants to replace high-GWP HFCs such as R32, R152a, R134a, R245fa, and R410A**. This target has been reached through an **energy, exergy, environmental, and techno-economic (4E) approach, implemented based on technical KPIs**, flammability, and legislative-economic considerations. This apparent progress toward technical and environmental compliance has unfolded an unexpected challenge; as the newly formulated refrigerants— whether HFOs, or blends—while less detrimental to climate change, often exhibit highly flammable characteristics compared to their predecessors. Overall, this paradigm shift is introducing significant safety challenges to be overcome [40,41] into the refrigeration industry of today, potentially elevating the cost of associated equipment and demanding a new level of awareness and preparedness. However, the proposed alternatives to current refrigerants have shown excellent compatibility and 4E performance in both simple **vapor-compression systems and advanced air conditioning configurations**. Promising retrofitting alternatives to CO_2 have also been tested, overcoming CO_2's safety limitations in sub-critical cascade cycles. **These findings offer key thermodynamic standpoints**, with specific, real-world applications explored throughout.

To tackle this challenge, the **polar soft-SAFT molecular based equation of state** was used for the **thermodynamic characterization of refrigerants**, fine-tuning the molecular parameters of **38 single-components including HFCs, HFOs, HCFOs, and aliphatic hydrocarbons** among others. Such parametrization achieved high accuracy, with average deviations consistently below 1.0% in saturated liquid density and, in most cases, below 3.0% in vapor pressure. The explicit inclusion of the **dipolar interactions** ensured a highly accurate and robust model, as demonstrated from **predicted first and second order thermodynamic derivative properties**. The **enthalpy of vaporization** closely matched experimental data with deviations under 3.0%, while single-phase densities aligned with molecular volumes, with R1233zd(E) exhibiting the lowest due to its size. Isobaric heat capacities were predicted within 5.0% of experimental values, with minimal errors within 1.0% observed for refrigerants like R601a and R1224yd(E). Some examples are highlighted in **Figures 2 and 3**.

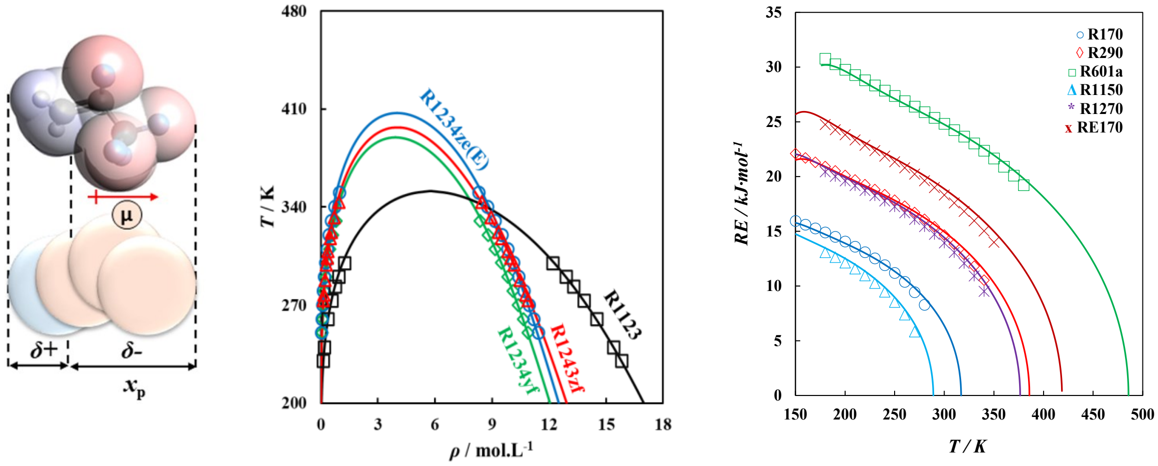

Figure 2. *From left to right. Soft-SAFT molecular coarse-grained model for a fluorinated refrigerant, VLE of selected HFOs, and prediction of enthalpies of vaporization, also referred to as the refrigeration effect (RE), crucial for subsequent calculations using pressure enthalpy (PH) and temperature entropy (TS) diagrams.*

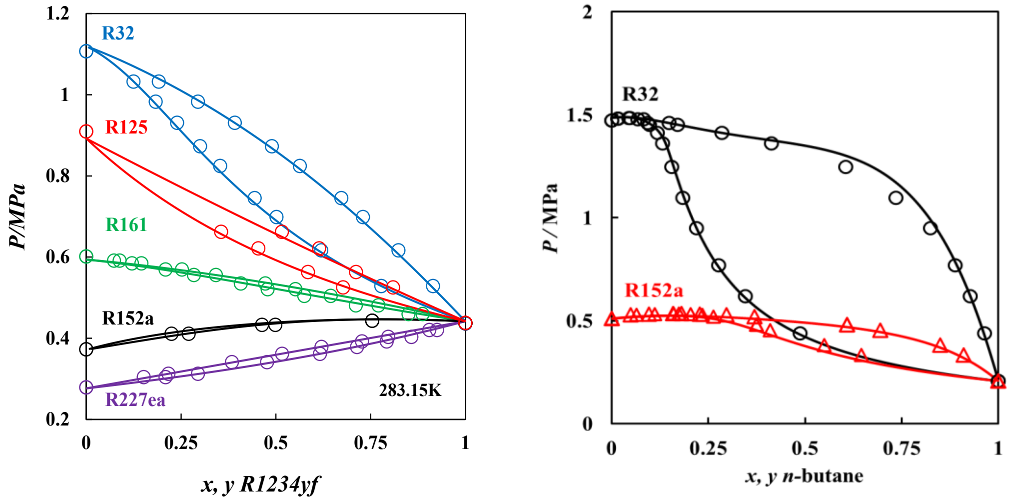

Figure 3. *Predicted VLE with binary interaction parameters set to one for F-based refrigerants (left) and n-butane + HFC mixtures at an isotherm of 293 K (right).*

Alternatively, another method for obtaining the saturation properties of refrigerants involved the use of artificial neural networks, with deviations for co-existing densities and vapor pressure of 1.63% and 6.59%, respectively. Lastly, the **polar soft-SAFT coarse-grain model demonstrated strong agreement with binary mixtures of polar + nonpolar azeotropic systems**, and multi-polar compounds, achieving average absolute deviations of approximately 1.0%. For CO_2-based blends, the SAFT coarse-grain models accurately predicted solubility profiles across multiple isotherms, requiring only minor adjustments to the energy binary parameter.

Further thermodynamic studies include the impact of lubricant leaks in the performance of a refrigeration cycle. A transferable **parametrization of two families of common lubricants such as Pentaerythritol Esters (PECs) and Polyethylene Glycol Dimethyl Ethers (PEGDMEs)** was carried out using soft-SAFT. From solubility calculations (see example in **Figure 4**), cycle efficiency studies were implemented and revealed that lubricant leaks (1-5% by weight) had a minimal impact on the energy efficiency of the cycle, with **PEC5 resulting in a coefficient of performance reduction of up to 3.0%, when paired with R513A**. In contrast, TrEGDME, the most effective PEGDME, caused up to a 5.7% reduction in *COP*, being more suitable for other type of refrigerants.

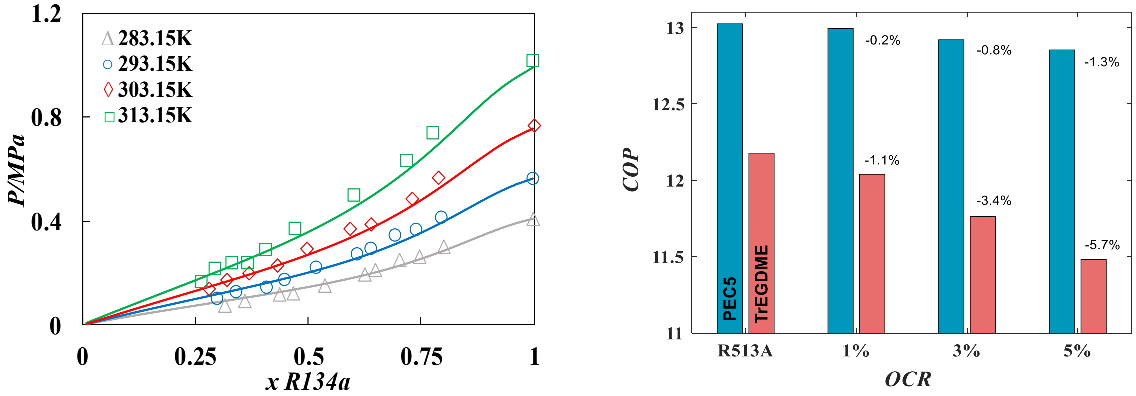

Figure 4. *Left: solubility prediction of the refrigerant R134a in TEGDME. Right: Impact of the oil circulation ratio (amount of lubricant leaked) on the cycle's coefficient of performance.*

The thermophysical behavior characterization served as a basis to perform a complete energy, exergy, environmental and economic 4E analysis to rapidly assess the **suitability of 4th generation refrigerants over their 3rd generation counterparts, based on efficiency, flammability, emissions and economic KPIs**. The study was first applied to a basic compression refrigeration cycle (VCRC), doing a pre-screening looking for pure compound alternatives. The drop-in analysis for R134a indicated that R1234yf and R1234ze(E) provided adequate Volumetric Cooling Capacity (*VCC*) values within 5% of R134a, though leading to up to a 3% decrease in the coefficient of performance. R1225ye(Z) showed a better balanced between performance and safety, with the added benefit of being non-flammable. Additionally, **R1123 was identified as the most compatible replacement but for R32, even though experiencing a 6.8% reduction in *COP***. For R152a, compatible alternatives included R1234yf, R1243zf, R1234ze(E), and R1225ye(Z), all reaching *VCC* values within 5% of R152a but up to a 5% reduction in *COP*, while no competitive alternatives were found for R410A, apart from the 3rd generation R32 compound. Finally, when replacing high-temperature application R245fa, R1336mzz(Z), R1224yd(Z), and R1233zd(E) were selected as promising choices, with R1224yd(Z) offering balanced performance, improved suction density, and specific heat capacity.

In a second stage, **the approach was extended to binary blends, with a focus on the two most common commercial refrigerants for drop-in, R134a and R410A**. For the former, **the mixture of HFOs R1243zf + R1234ze(E) (60/40) *wt.*% stood out as the most promising option, offering 90% compatibility, a GWP of 30, high efficiency, and energy and exergy performance nearly identical to R134a (see mixture 5** in **Figure 5)**. Concerning R410A, R1123 + R32 (90/10) *wt.*%, was found to be 73% compatible with R410A, comparable to R32, with a *VCC* at 90% of R410A, and a slightly higher discharge line temperature, highlighting the need for careful adjustments during retrofitting. The techno-economic analysis further demonstrated the need of raising taxes on HFC and carbon emissions to enhance the appeal of such low-GWP alternatives, with the former blend showing the most significant improvement in cost-effectiveness under higher tax rates. Similarly, blend R1123 + R32 (90/10) *wt.*% required only a 3.2-fold increase in the HFC tax to align its annual costs with those of R410A.

Thermodynamic properties and performance metrics		
Normal Boiling Point (*NBP*)	T_{atm}^{SAT}	
Pressure Ratio (P_R)	$P_{cond} \cdot P_{evap}^{-1}$	*min**
Power Per Ton of Refrigeration (*PPTR*)	$3.5167 \cdot COP^{-1}$	
Suction Density (ρ_V)	ρ_1	
Refrigeration Effect (*RE*)	$H_1 - H_3$	
Coefficient of Performance (*COP*)	$\frac{CC}{\dot{W}} = \frac{RE}{\omega_c}$	*max**
Exergetic Efficiency (η_{II})	$1 - \left(\frac{\sum \dot{X}_d}{\sum \dot{X}_{in}}\right)$	

* *Variation to HFCs*

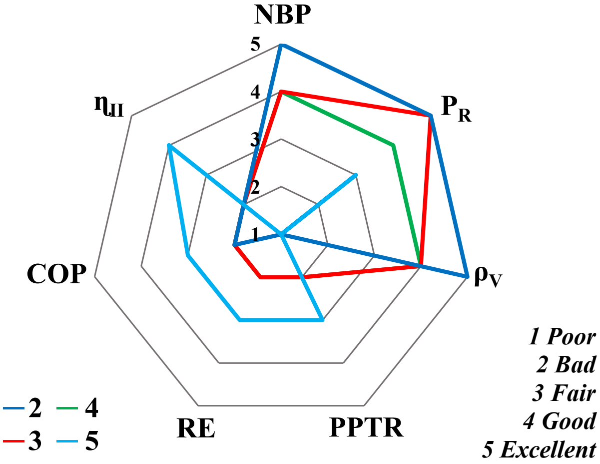

Figure 5. *Left: summary of key performance indicators used to evaluate new refrigerants. Right: Performance of the new proposed blends referred to R134a:* ***2*** *(90/10)wt.% R1234yf + R134a* ***3*** *(90/10)wt.% R1234yf + R152a* ***4*** *(80/20)wt.% R1234yf + R152a* ***5*** *(60/40)wt.% R1243zf +R1234ze(E).*

A statistical analysis built on the use of soft-SAFT was adopted to evaluate the effect of **design factors on the energy and exergy performance of such air-conditioning cooling cycles**. Using a two-level design of experiments (DoE) with a fractional factorial design resolution, supported by an analysis of variance and a polynomial response regression, the analysis ranked the design factors in descending order of importance as follows: *Condensing Temperature >> Isentropic Compression >> Evaporating Temperature > Refrigerant-type > System-type > Superheating > Subcooling Temperature*. Further optimization using a three-level DoE enhanced heat transfer in the intercooler unit, resulting in a 21% increase in exergy efficiency, annual cost savings of $1,590 due to high pinch point and a reduction in CO_2 emissions by 1.02 tons over a 15-year lifespan.

Furthermore, the impact of advanced cooling cycle configurations was evaluated using the same methodology. Results show that t**he use of liquid-to-suction line heat-exchanger (LL/SL-HX) cycles holds significant annual cost savings of $39 to $116 per unit, compared to the basic VCRC**. In contrast, two-stage linear compressor (TS-VCRC) systems offer considerable advantages in terms of energy and exergy efficiencies, with the potential for further enhancements through fine-tuning operating conditions. This results in improved energy and exergy efficiencies for all working fluids, along with a higher avoidable exergy rate. However, it comes with the trade-off of higher total annual costs, which increase by 8.0 to 10.0%, or $66.5 to $73.0 annually per unit, compared to the basic configuration. Despite the substantially higher CAPEX, the multi-compressor ensemble is more favorable in terms of energy, exergy, and environmental, especially when deployed as a new system. The study in advanced cycles using the new proposed working fluids was completed by a detailed **Life Cycle Analysis (LCA)**, focused on CO_2-eq emissions. The LCA revealed that the choice of refrigerant was the primary factor influencing GWP reduction, though. Specifically, replacing R410A with R1123 + R32 (90/10) *wt.*% blend in a multi-compressor cycle led to a 23.7% decrease in GWP, while replacing R134a with blend R1243zf + R1234ze(E) (60/40) *wt.*%, from basic to a TS-VCRC mode resulted in an 18.6% reduction. By 2050, **the prospective LCA assessment confirmed that high-GWP refrigerants will contribute more than 40% to GWP through direct and indirect emissions and production environmental costs, but can be mitigated to 10% or less with low- and mid-GWP agents**.

The last part of the PhD thesis was focused on ultra-low temperature refrigeration and, in particular, on finding **suitable CO_2-based refrigerant mixtures for replacing pure carbon dioxide in sub-critical cascade applications**. The lack of flammability data was overcome by developing an **innovative ANN model, based on σ-profiles from COSMO-RS as input descriptors, to predict the flammability classes of untested refrigerant blends**. The ANN architecture demonstrated exceptional predictive performance, with metrics such as a coefficient of determination of 0.999, root mean square error of 0.1735, average absolute relative deviation of 0.8091%, average standard deviation of ± 0.0434, and 81.3% of the dataset with standardized residuals of ±1. Further validation was achieved through the Applicability Domain (AD) analysis, demonstrating that 97.67% of the total 3D space was within the AD, a coverage that extends to 99.36% when considering borderline outliers. Additionally, **a second ANN-based model in Figure 6 was also developed to predict the vapor-liquid equilibria of CO_2-based mixtures with no experimental data**, in order to have the required information for the energy/exergy calculations. The multitask model, based on the same type of descriptors, achieved high accuracy, with average absolute relative deviations under 3.5% for liquid and vapor phases, effectively handling 531 data combinations and showing minimal performance decline in dew phase predictions above 300 K. Outlier percentages for **bubble and dew phase predictions were 2.63% and 2.44%,**

respectively, confirming the model's overall accuracy and effectiveness. Following thorough validation, the flammability and thermophysical properties of CO_2-based mixtures was considered, resulting in the identification of 43 mixtures that met the required environmental, technical, and safety criteria. Twelve mixtures outperformed pure CO_2 in energy and environmental performance, 42 demonstrated superior exergy efficiency, and 11 showed improved economic prospects. **Mixture 21 [(80/20) *wt.*% R1123 + CO_2] was particularly notable for its high *COP* and Total Equivalent Warming Impact (*TEWI*) rankings, while mixtures (10/90) *wt.*% R1243zf + CO_2 and (10/90) *wt.*% R1225ye(Z) + CO_2 excelled in exergy efficiency despite lower overall performance**.

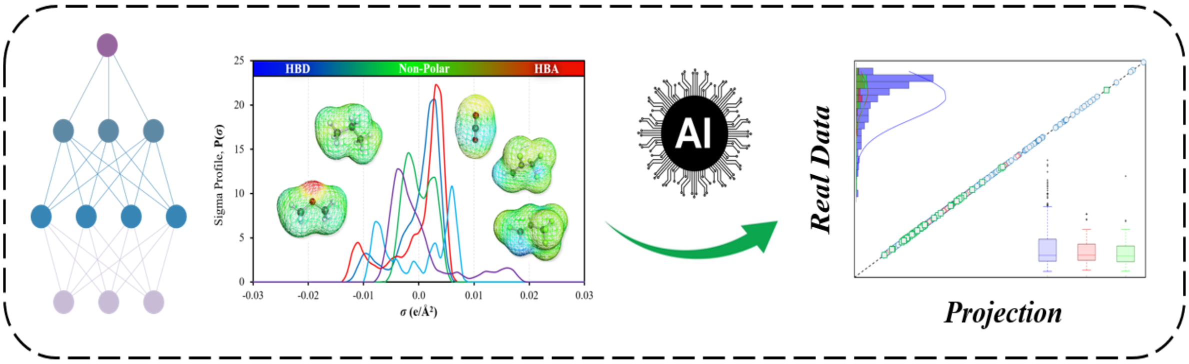

Figure 6. *ANN-based framework to predict thermodynamic properties of novel blends.*

The main findings of this PhD can be summarized in the following bullets:

- The **polar soft-SAFT** model has been used to describe the thermophysical properties of 38 refrigerants, achieving an average deviation of 0.8% for liquid density and 2.5% for vapor pressure.
- The **effect of the lubricants** in cycles has been studied based on **solubility and miscibility**: PEC5 caused a 3.0% reduction in *COP* when used with R513A, while TrEGDME resulted in a 6.1% *COP* reduction with other refrigerants, indicating minimal energy efficiency loss from lubricant leaks.
- A complete drop-in analysis, based on **key performance indicators coming from thermodynamic calculations**, were used to evaluate replacements for common high GWP systems R134a and R410A. Blend **R1243zf + R1234ze(E) (60/40) *wt.*%** achieved 90% compatibility with R134a and a GWP of 30. However, R1123 + R32 (90/10) *wt.*% was 73% compatible with R410A.
- Advanced Cycles: LL/SL-HX cycles provided annual cost savings of $39 to $116 per unit compared to VCRC. TS-VCRC improved energy efficiency but increased costs by 8% to 10%.

Overall, the collective results presented herein not only demonstrate the **ability of the proposed approach, built on multi-scale molecular modeling, but also assists in rapidly examining the inherent trade-offs and potential challenges in selecting the next generation of refrigerants for climate change mitigation**. As such, **the role of thermodynamics is at the core of this work, providing solutions to industrial challenges to reach the sustainability goals**.

References

[1] Assessing the Global Climate | News | National Centers for Environmental Information (NCEI).
[2] FacilityExecutive, The Future Of Cooling.
[3] IEA, The Future of Cooling – Analysis - IEA.
[4] Climate Central, Hotter Climate, Higher Cooling Demand | Climate Central.
[5] IEA, Cooling - Fuels & Technologies - IEA. 2022.
[6] M.O. McLinden, M.L. Huber, J. Chem. Eng. Data 65(9) (2020) 4176–93. 10.1021/acs.jced.0c00338.

[7] G. Raabe, Fluid Phase Equilib. 485 (2019) 190–8. 10.1016/j.fluid.2018.12.022.
[8] N. Abas, A.R. Kalair, N. Khan, A. Haider, Z. Saleem, M.S. Saleem, Renew. Sustain. Energy Rev. 90 (2018) 557–69. 10.1016/j.rser.2018.03.099.
[9] J.M. Calm, D.A. Didion, Int. J. Refrig. 21(4) (1998) 308–21. 10.1016/S0140-7007(97)00089-3.
[10] Z. Yang, B. Feng, H. Ma, L. Zhang, C. Duan, B. Liu, Y. Zhang, S. Chen, Z. Yang, Int. J. Refrig. 126 (2021) 12–22. 10.1016/j.ijrefrig.2021.01.022.
[11] V. Nair, Int. J. Refrig. 122 (2021) 156–70. 10.1016/j.ijrefrig.2020.10.039.
[12] IPCC, in: V. Masson-Delmotte, P. Zhai, Y. Chen, L. Goldfarb, M. I. Gomis, J. B. R. Matthews, S. Berger, M. Huang, O. Yelekçi, R. Yu, B. Zhou, E. Lonnoy, T. K. Maycock, T. Waterfield, K. Leitzell, N. Caud, Climate Change: The Physical Science Basis, Cambridge University Press, 2021,
[13] B.K. Sovacool, S. Griffiths, J. Kim, M. Bazilian, Renew. Sustain. Energy Rev. 141 (2021) 110759. 10.1016/j.rser.2021.110759.
[14] UN Environment Ozone Secretariat, United Nations Environ. Program. (2017).
[15] EU, (2016).
[16] M. Schulz, D. Kourkoulas, Off. J. Eur. Union 2014(517) (2014) https://doi.org/10.4271/1999-01-0874.
[17] A. Mota-Babiloni, J. Navarro-Esbrí, P. Makhnatch, F. Molés, Renew. Sustain. Energy Rev. (2017) 1031–42. 10.1016/j.rser.2017.05.216.
[18] D. Wu, B. Hu, R.Z. Wang, Renew. Sustain. Energy Rev. 138 (2021). 10.1016/j.rser.2020.110571.
[19] A. Kazakov, M.O. McLinden, M. Frenkel, Ind. Eng. Chem. Res. 51(38) (2012) 12537–48. 10.1021/ie3016126.
[20] M.O. McLinden, J.S. Brown, R. Brignoli, A.F. Kazakov, P.A. Domanski, Nat. Commun. 8(1) (2017) 14476. 10.1038/ncomms14476.
[21] C.G. Albà, I.I.I. Alkhatib, F. Llovell, L.F. Vega, ACS Sustain. Chem. Eng. 9(50) (2021) 17034–48. 10.1021/acssuschemeng.1c05985.
[22] B.O. Bolaji, Z. Huan, Renew. Sustain. Energy Rev. 18 (2013) 49–54. 10.1016/j.rser.2012.10.008.
[23] P. Giménez-Prades, J. Navarro-Esbrí, C. Arpagaus, A. Fernández-Moreno, A. Mota-Babiloni, Renew. Sustain. Energy Rev. 167 (2022) 112549. 10.1016/j.rser.2022.112549.
[24] S. Karagoz, M. Yilmaz, O. Comakli, O. Ozyurt, Energy Convers. Manag. 45(2) (2004) 181–96. 10.1016/S0196-8904(03)00144-4.
[25] J.L.C. Fannou, C. Rousseau, L. Lamarche, S. Kajl, Appl. Therm. Eng. 82 (2015) 306–17. 10.1016/j.applthermaleng.2015.02.079.
[26] A. Khalid Shaker Al-Sayyab, A. Mota-Babiloni, J. Navarro-Esbrí, Energy Convers. Manag. 228 (2021). 10.1016/j.enconman.2020.113703.
[27] A. Mota-Babiloni, J.M. Belman-Flores, P. Makhnatch, J. Navarro-Esbrí, J.M. Barroso-Maldonado, Energy 162 (2018) 99–110. 10.1016/j.energy.2018.08.028.
[28] T. Halon, B. Gil, B. Zajaczkowski, Appl. Therm. Eng. 210 (2022) 118354. 10.1016/j.applthermaleng.2022.118354.
[29] G. Bamorovat Abadi, K.C. Kim, Renew. Sustain. Energy Rev. 73 (2017). 10.1016/j.rser.2017.02.020.
[30] R. Llopis, D. Sánchez, R. Cabello, J. Catalán-Gil, L. Nebot-Andrés, Int. J. Refrig. 84 (2017) 52–66. 10.1016/j.ijrefrig.2017.08.022.
[31] P. Makhnatch, A. Mota-Babiloni, R. Khodabandeh, Int. J. Refrig. 84 (2017) 26–35. 10.1016/j.ijrefrig.2017.08.010.
[32] A. Mota-Babiloni, J. Navarro-Esbrí, A. Barragán-Cervera, F. Molés, B. Peris, Energy 90 (2015) 1636–44. 10.1016/j.energy.2015.06.133.
[33] C. Aprea, A. Greco, A. Maiorino, Int. J. Refrig. 82 (2017) 71–82. 10.1016/j.ijrefrig.2017.07.001.
[34] C. Aprea, A. Greco, A. Maiorino, Appl. Therm. Eng. 141 (2018) 226–33. 10.1016/j.applthermaleng.2018.02.072.
[35] K. Harby, Renew. Sustain. Energy Rev. 73 (2017) 1247–64. 10.1016/j.rser.2017.02.039.
[36] V. Oruç, A.G. Devecioğlu, Int. J. Refrig. 128 (2021) 242–51. 10.1016/j.ijrefrig.2021.04.007.
[37] A. Mota-Babiloni, J. Haro-Ortuño, J. Navarro-Esbrí, Á. Barragán-Cervera, Int. J. Refrig. 91 (2018) 136–45. 10.1016/j.ijrefrig.2018.05.018.
[38] R. Llopis, D. Calleja-Anta, D. Sánchez, L. Nebot-Andrés, J. Catalán-Gil, R. Cabello, Int. J. Refrig. 106 (2019) 133–43. 10.1016/j.ijrefrig.2019.06.013.
[39] K. Thu, K. Takezato, N. Takata, T. Miyazaki, Y. Higashi, Int. J. Refrig. 121 (2021) 289–301. 10.1016/j.ijrefrig.2020.10.009.
[40] M. Walid Faruque, M. Hafiz Nabil, M. Raihan Uddin, M. Monjurul Ehsan, S. Salehin, Energy Convers. Manag. 14 (2022) 100207. 10.1016/j.ecmx.2022.100207.
[41] S. Kujak, K. Schultz, Sci. Technol. Built Environ. 22(8) (2016) 1226–37. 10.1080/23744731.2016.1203239.