# Applications of Vaporizer in Atmospheric Gas and Heating TEM

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## Introduction

Water's negative effects on metal corrosion[1] and catalyst deactivation[2] are well known and under study for decades. On the positive side, water can act as reactants in hydrogen production reactions, like water-gas shift reaction[3] (water is also a product in reverse water-gas shift reaction (RWGS)). With the introduction of aberration correctors, in-situ and operando gas and heating TEM can reveal structure and composition down to atomic resolution in their working status. However, the investigations on water's influence to gas-solid reactions at atmospheric environment inside a TEM are limited due to limited control over the water vapor flow and fear of potential leak to contaminate the TEM columns. In this work, we will present two application examples of our recently developed vaporizer for MEMS-based gas and heating TEM. One is the FeCrAl alloy corrosion and the other is water's influence on NiAu nanoparticles for RWGS.

## Experimental set-ups

DENSsolutions' Climate G+ system, including 3 feeds GSS, TEM sample holder, vaporizer componnets between GSS and TEM holder, gas and heating nano-reactor and Impulse software, DENSsolutions gas analyzer, and a Thermo-Fisher Themis ETEM operated at 300 kV were used in this work.

As shown in Figure 1, the vaporizer component is allocated on the position directly before the TEM holder, where gas pressure and flow rate controller located. This design delivers benefits of no contamination to dry gas supply, fast and wide range of water partial pressure switch (0 to 100% relative humidity (RH)), flexible wet gas pressure and flow rate control and so on.

FeCrAl alloy was firstly cut and thinned by focused ion beam and then transferred to Climate nano-reactor. NiAu nanoparticles were firstly dissoved in ethanol and then transferred to the Climate nano-reactor by drop-casting.

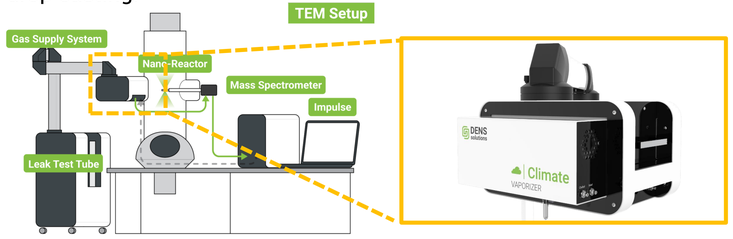



**Figure 1** Schematic view of operando gas and heating TEM set-up. Vaporizer's location was marked in orange color and magnified on right.

## Results and Discussion – FeCrAl Alloy

FeCrAl alloy, a potential alternative material to Zr alloy in nuclear fuel cladding, features better corrosive-resistance and oxidation-resistance under high temperature vapor environment. In this work, we investigated FeCrAl alloy's structure and composition change under controlled vapor environment.

As shown in Figure 2, under the flow of 100 % RH water vapor carried by inert gas He, the bright field image shows elliptical features of water bubble formation at 400 °C. Increase of the temperature from 400 to 500 °C triggers the growth of oxide grains. These grains transformed to one dimensional wire/rod features upon further temperature increase, as can be seen in 700 °C image. These one dimensional features will move, grow and detach and left final $Al_2O_3$ large grains, as shown in 1200 °C images. Note, structure changes immediately upon temperature increase. Here we only show final stable status at each temperature. Dynamic views are shown in the video.

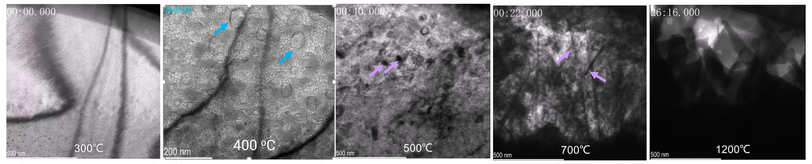
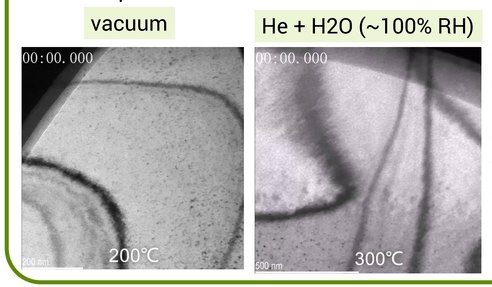



**Figure 2** FeCrAl alloy Structure change over temperature increase under 100% RH water vapor condition at a flow rate of 0.3 mln/min.




As revealed by the videos, without water, the material only involves sintering and crystallization under thermal treatment. With water, the alloy oxidizes in a very dynamic way and reveals detailed process of the oxidation.

**Video** Comparison of FeCrAl alloy changes without and with water.

## Conclusions

Development and application of such vaporizer are expected to help design more sustainable metal materials and catalysts from fundamental failure mechanism studies.

## References

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2 Goguet et.al., Deactivation Mechanism of a Au/$CeZrO_4$ Catalyst During a Low-Temperature Water Gas Shift Reaction, J. Phys. Chem. C 2007, 111, 45, 16927-16933
3 Ebrahimi et.al., A review of recent advances in water-gas shift catalysis for hydrogen production, Emergent Materials 2020, 3, 881-917

## Results and Discussion – NiAu Nanoparticles

A Ni-Au catalytic system, which has highly selective CO production (against $CH_4$) in $CO_2$ hydrogenation. In-situ ETEM analysis proves that the catalytic performance is contributed by the formation of a transient reconstructed alloy surface, promoted by CO adsorption during the reaction, rather than the Au shell (Ni core) reveal from ex-situ analysis.

To understand the mechanisms driving the alloy structure formation, the involved gas are introduced to gas environment one by one or in pairs.

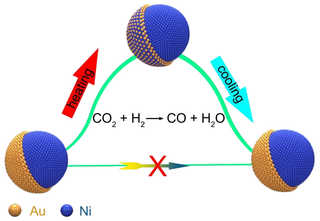


**Figure 3** Schematic view of Ni-Au structure evolution path.

As shown in Figure 4, *pure $H_2$ environment* maintains initial Au@Ni core-shell structure. *Introducing in about 100% RH water vapor* leads to Ni and Au phase separation and loose NiO outer layer. *Only water vapor about 100% RH* turns the outer NiO layer from loose to condesed. Moreover, $H_2$ plus about 25% RH water vapor turns the Ni-Au phase separated structure to change reversibly between with and without NiO loose layer. Further interpretation are under study.

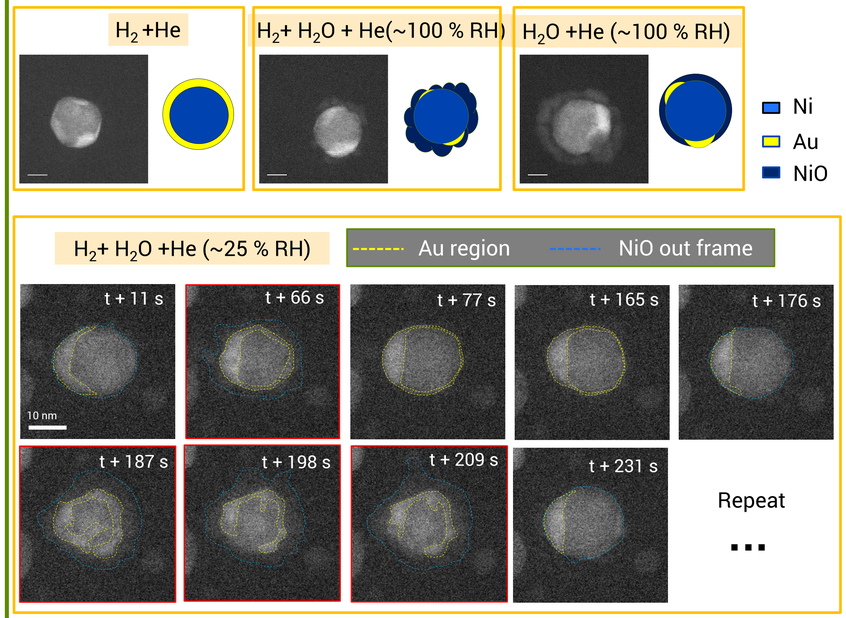


**Figure 4** Ni-Au nanoparticle structure evolution under different gas environment. The composition were concluded from HRTEM and EDS mapping.

# Live scanning ptychography with the LiberTEM software framework

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## Live 4D STEM data processing and plotting

- Any combination of user-defined functions
- Wide range of algorithms possible: Virtual detectors, differential phase contrast, ptychography,  strain and orientation mapping, …
- Both CPU and GPU
- Example: Live single side band ptychography (SSB) and first moment analysis
- Available as Open Source (GPL-3)
- Gatan K2 IS support under development (prototype)
- Parallel/distributed live processing soon

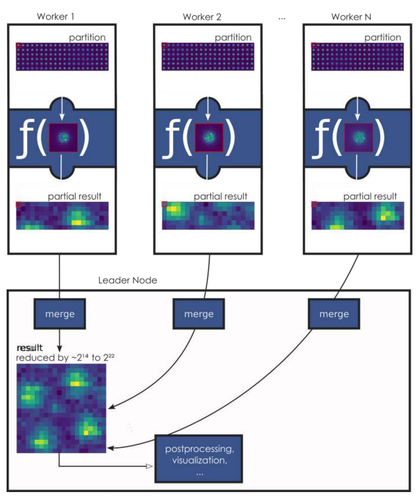
## More information, example notebooks, downloads

- https://ptychography-4-0.github.io/ptychography/
- https://libertem.github.io/LiberTEM/
- https://libertem.github.io/LiberTEM-live/

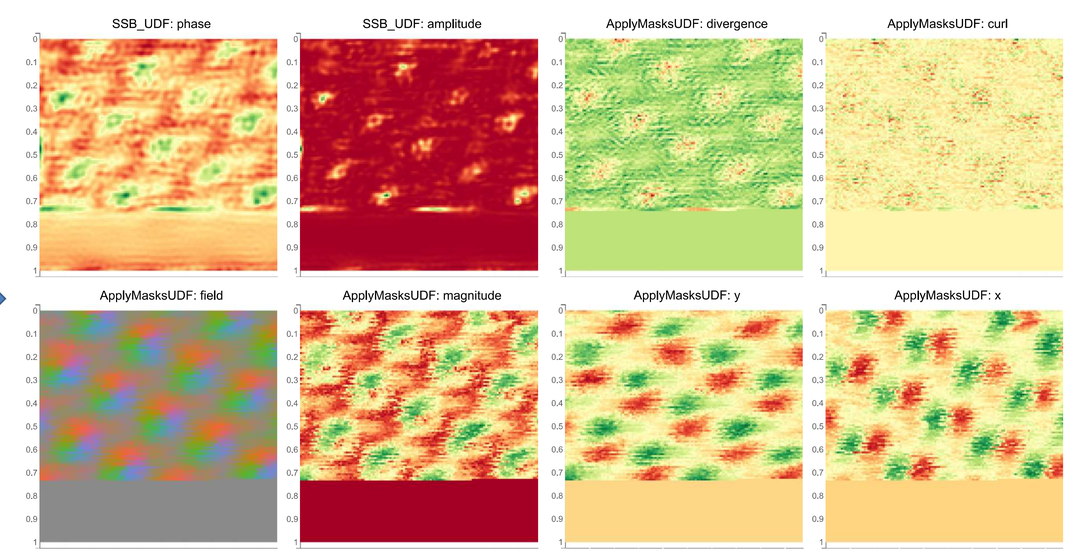
- arXiv:2106.13457
- Contact: d.weber@fz-juelich.de

```
In [25]: c = MerlinControl(*MERLIN_CONTROL_SOCKET)

print("Connecting Merlin control...")
with c:
    merlin_setup(c)
    microscope_setup()

    set_nav(c, aq)
    arm(c)
try:
    ctx.run_udf(dataset=aq, udf=[ssb_udf, com_udf], plots=plots)
finally:
    try:
        if acquisition_state.trigger_result is not None:
            print("Waiting for blocking scan function...")
            print(f"result = {acquisition_state.trigger_result.result()}")
    finally:
        pass #microscope.stop_scanning()
print("Finished.")
```


Quantum Detectors
MerlinEM




LiberTEM




Combination of user-defined routines:
Here SSB and first moment analysis

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- We gratefully acknowledge funding from the Initiative and Networking Fund of the Helmholtz Association within the Helmholtz Young Investigator Group moreSTEM under Contract No. VH-NG-1317

# 3D Electron Diffraction/Micro-ED for Structural Characterization of beam sensitive Loratadine and Linagliptin APIs using Pixelated detectors

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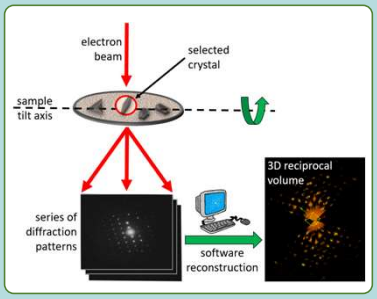
## Introduction

In recent years, the scientific community has shown a renewed interest in use of 3D Electron Diffraction (3D-ED)/Micro Electron Diffraction (Micro-ED) for characterization of pharmaceutical compounds. For many API's (active pharmaceutical ingredient), it is always challenging to grow suitable size crystals for single crystal X-ray diffraction. Powder X-ray Diffraction (PXRD) has its own challenges e.g. (a) low crystallinity of the sample, which produces a broadening of peak profiles (b) long cell parameters and pseudo symmetries, which lead to peak overlap even at low and medium resolution (c) presence of minor impurities or polymorphic forms. In all those cases, 3D-ED/Micro-ED in Transmission Electron Microscope (TEM) could be a useful alternative for structural studies, as crystals as small as 50 nm can be studied.

## Principle of 3D ED data collection in TEM

The principle of acquiring 3D-ED data consists on focusing the electron beam on a nm size crystal in TEM/STEM mode and sampling the reciprocal space in small steps (usually 1 degree tilt or less) using beam precession or using continuous rotation (Micro-ED with or without beam precession) of the crystal.

As organic crystals are often very beam sensitive, data collection can be done either at room temperature and/or at cryo-conditions using pixelated detectors at low dose conditions (< 0.01e/Å$^2$/ sec) at STEM mode. The acquired 3D-ED data can be processed to determine *ab-initio* unit cell, space group, atomic positions and moreover, hydrogen atom positions can also be determined [1].




## Case Studies 1: Carbamazepine Structure

Carbamazapine (CBZ) is primarily used in the treatment of epilepsy and neuropathic pain. It may be used in schizophrenia along with other medications and as a second-line agent in bipolar disorder. CBZ exists in several polymorphic forms.

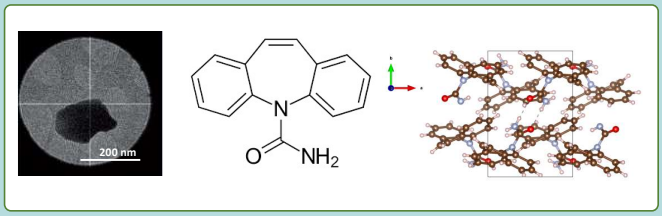



*Figure 1. TEM Image of the carbamazepine nanocrystal and ab-initio solved structure from 3D-ED data at RT [2].*

| Experimental 3D-ED Unit Cell (RT) | Literature Reported (SCXRD-RT) |
|---|---|
| a = 7.68 Å | a = 7.534 Å |
| b = 11.44 Å | b = 11.150 Å |
| c = 13.92 Å | c = 13.917 Å |
| β = 91.22° | β = 92.94° |
| **SPG: P21/n** | **SPG: P21/n** |

## Case Studies 2: Ramelteon Structure

Ramelteon is the first selective melatonin MT1 and MT2 receptor agonist approved by the U.S. Food Drug and Administration (FDA) in 2005 for the treatment of insomnia.

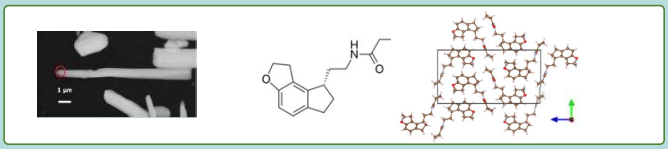



*Figure 2. TEM Image of the Ramelteon crystals and solved structure from 3D-ED data at RT by Simulated Annealing [3].*

| Experimental 3D-ED Unit Cell (RT) | Unit cell from SCXRD study (RT) |
|---|---|
| a = 4.99 Å | a = 5.0450 (4) Å |
| b = 11.59 Å | b = 12.4178 (11) Å |
| c = 22.95 Å | c = 23.187 (2) Å |
| **SPG: $P2_12_12_1$** | **SPG: $P2_12_12_1$** |

## Case Studies 3: Loratadine Form II Structure

Loratadine, available under the brand name Claritin among others, is a medication used to treat allergies. Loratadine exists in two different polymorphic forms.

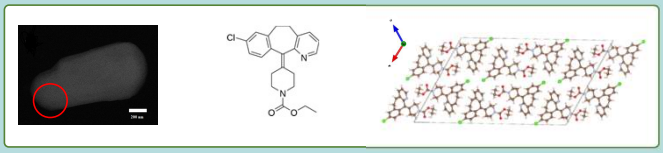



*Figure 3. TEM Image of the metastable Loratadine Form II crystal and solved structure from 3D-ED data at RT by Simulated Annealing [4]*

| Experimental 3D-ED Unit Cell (RT) | Literature Reported Unit cell (SCXRD-LT) |
|---|---|
| a = 35.41 Å | a = 35.652(10) Å |
| b = 5.28 Å | b = 5.206(2) Å |
| c = 22.56 Å | c = 22.743(6) Å |
| β = 118.21° | β = 117.418(14)° |
| **SPG: C2/c** | **SPG: C2/c** |

## Case Studies 4: Linagliptin Structure

Linagliptin, sold under the brand name Tradjenta among others, is a medication used to treat diabetes mellitus type 2. As of now 30 polymorphs of Linagliptin are known to exist. Our current structure matches closely with one of the patented form of which no structure was previously reported.

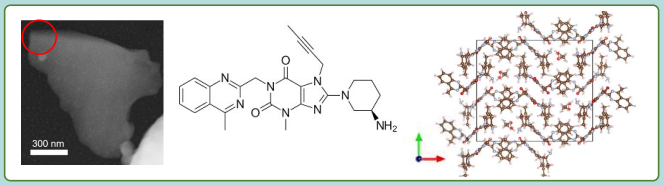



*Figure 4. TEM Image of the Linagliptin crystal and ab-initio solved structure from 3D-ED data at RT [5]*

| Experimental 3D-ED Unit Cell (RT) | Unit Cell from Synchrotron data (RT) |
|---|---|
| a = 24.85 Å | a = 24.85091(13) Å |
| b = 21.57 Å | b = 21.56916(9) Å |
| c = 9.74 Å | c = 9.74376(4) Å |
| **SPG: $P2_12_12$** | **SPG: $P2_12_12$** |

## Conclusions

Our results show that 3D-ED/Micro-ED techniques in combination with Direct Detection cameras can be used as a powerful tool for phase identification and structural characterization for nm size (50-500 nm) beam sensitive pharmaceutical materials.

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